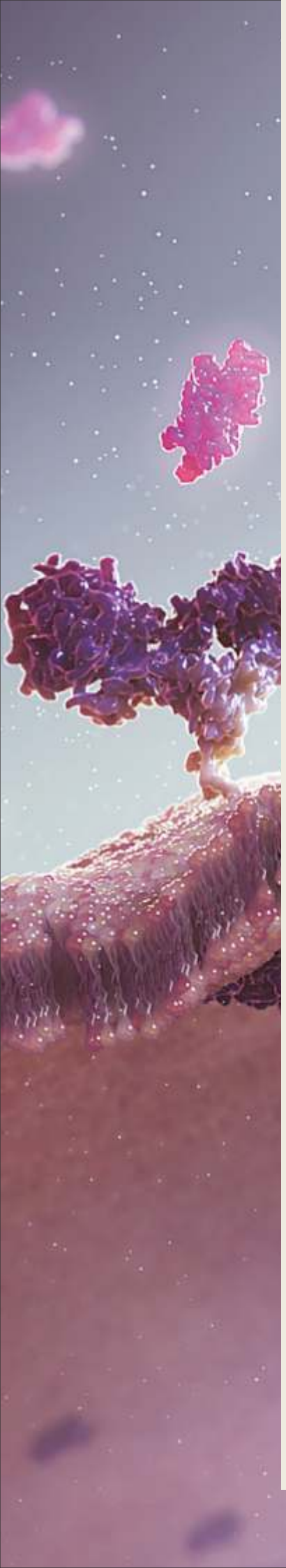


I-OSI Newsletter
Inaugural Issue
Nov 2018

IMMUNO-ONCOLOGY SOCIETY OF INDIA

Welcome Address

Dear Friends,

In Persian culture, the winter solstice is called Yaldā (meaning: birth) and has been celebrated for thousands of years as the eve of the birth of Mithra, who symbolized light, goodness and strength on earth.

It is therefore so apt to bring out the inaugural issue of the I-OSI newsletter this time of the year and hope this will give "birth" to many productive and fruitful endeavors in future.

As some of you are aware, the Immuno-oncology Society of India (I-OSI) was launched by adoption of the "Mumbai Resolution" on February 24th, 2018 in Mumbai with a view to promote and advance the scientific knowledge and research in Immuno-oncology.

We all know that Immuno-oncology cuts across cancer sites and the interest group includes basic scientists and oncologists from all specialties including the whole spectrum of solid tumours as well as Hematolymphoid Malignancies. Although ancient, Immuno-oncology is reinvented in this era and is growing at a fast pace and indications are advancing almost every fortnight.

I-OSI would hopefully serve as a platform for all interested members to share, learn and further advance our understanding of Immuno-oncology so as to help the ultimate beneficiary- our patients in India, even better. The concept and evolution of the society is elaborated in the 'Secretary speaks' column.

The most important immediate agenda is of course the inaugural annual conference of I-OSI, which will be held in Tata Memorial Centre, Mumbai from March 15-17, 2018.

Details of the conference can be found on the conference website www.immunooncologyindia.com. I would request all of you to not only attend the conference but also spread the message across to all your colleagues, trainees, fellows, and all other personnel who you think may be interested.

The Patrons of the meeting are Dr R A Badwe, and Dr S Chiplunkar, Dr SD Banavali and Dr Atul Sharma are the chair of the meeting and Dr R Jalali and Dr K Prabhash are the scientific chairs and Dr G Narula is the treasurer.

I the organizing secretary, and the entire team, are working hard to organize a world class conference for you. For this meeting, highly eminent national and international faculties have been roped in and we feel it would be an academic treat for all and well worth attending.

All the relevant information about the I-OSI is mentioned on our website www.immunooncologyindia.com However, we welcome your thoughtful suggestions for the website to make it more meaningful. Furthermore, I also request you to become the members of the society. A copy of the membership form is enclosed with this newsletter and it can be also downloaded from the I-OSI website. You will also find a detailed 'Members' directory on the website.

We have included a list of important national and international conferences related to Immuno-oncology as well as a list of useful websites in this inaugural issue. I am sure, subsequent issues will be with addition of more useful and interesting columns.

Looking forward to seeing you all at the I-OSICON19 in March.

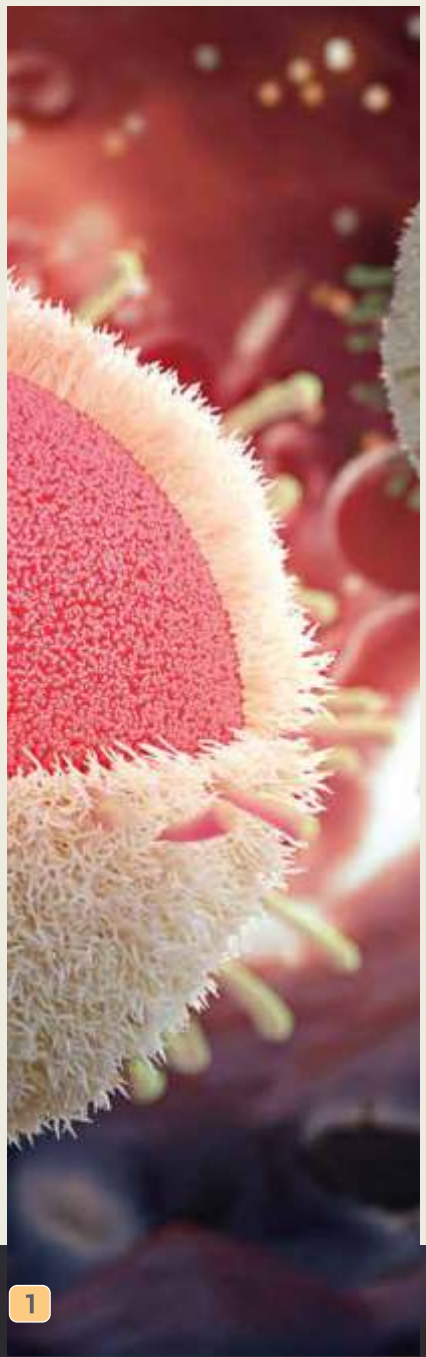
Warm Regards,

Dr.Jyoti Bajpai
Organizing Secretary

Immuno-Oncology Society Of India, Annual conference 2019

President's Message

Dr. Shubhada Chiplunkar
Director, Advanced Centre for Treatment,
Research and Education in Cancer (ACTREC),
Navi Mumbai, Maharashtra



Dear I-OSI Members,

During the past decade anti-cancer immunotherapy has evolved from a promising therapeutic option to robust reality that has changed treatment outcomes. The development of cancer vaccines, CAR-T cells, and checkpoint inhibitors are changing the paradigms of clinical cancer management. Immunotherapy is rapidly evolving cancer treatment modality with exciting benefits but also poses unique challenges for patients and the healthcare team. Clinical studies are being initiated at an accelerating pace to test the safety and efficacy of various immunotherapeutic regimens in cancer patients, either as stand alone interventions or combined with radiotherapy, antineoplastic agents or epigenetic modulators.

Cancer Immunotherapy is nascent in India. The Immuno-Oncology Society of India (I-OSI) was established with the aim to increase public awareness about immunotherapies, boost basic and clinical research on immune-oncology and provide a forum for interdisciplinary interactions between physicians and scientists. The I-OSI will be a forum to connect basic scientists working in immunology with clinicians to bring lab discoveries to bedside. I-OSI will aim to keep all the stakeholders up-to-date in this rapidly evolving field.

Progress made in human genome sequencing and bioinformatics, detection and understanding of genetic and epigenetic information of tumors and immune landscapes will help to establish individualized immunotherapy to obtain clinical benefits for more patients.

As the number of immune therapies are expected to rise in the foreseeable future, there are several key issues that remain and require further investigation in order to optimize the anti-cancer potential of this class of agents. Primary and acquired resistance becomes one of the major obstacles, which greatly limits the long lasting effects and wide application of cancer immunotherapy.

In order to optimize benefit and minimize risk there is an urgent need to have predictive biomarkers, identify hyperprogressors, understand the mechanisms of resistance and immune related toxicities, decide treatment duration and clinical trial design.

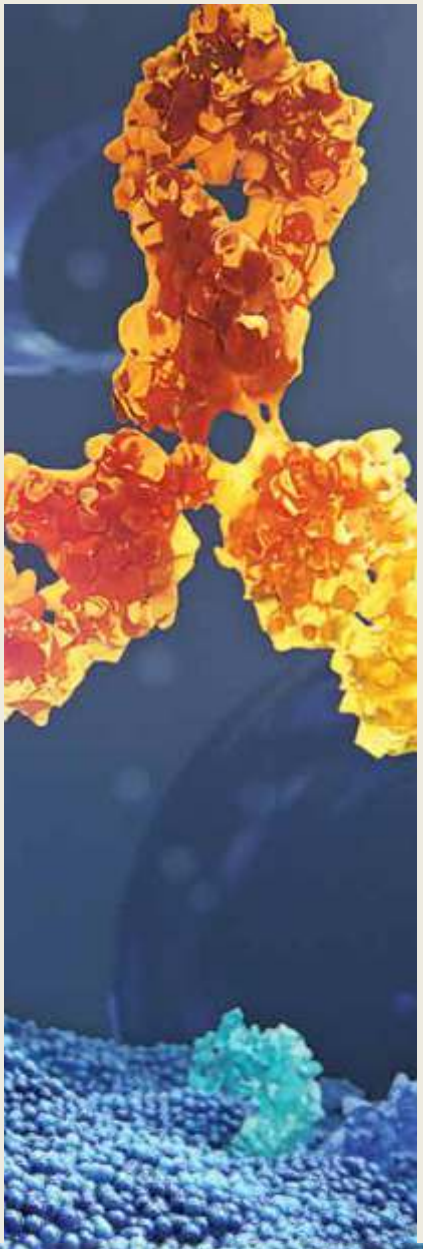
It gives me great pleasure to present the first issue of the I-OSI Newsletter. I take this opportunity to invite all the I-OSI members to actively contribute to the newsletter by sharing their thoughts and expertise that will create new linkages and foster opportunities for networking.

Warm Regards,

Dr. Shubhada Chiplunkar
President
Immuno-Oncology Society Of India

Secretary Speaks

Dr. Jyoti Bajpai
Professor, Medical Oncology,
Tata Memorial Centre,
Mumbai, Maharashtra



"A journey of a thousand miles begins with a single step."

In India, cancer immunotherapy is at a nascent stage and mostly dependent on import and adoption of technologies and drugs patented in the more developed countries. India, with its huge cancer burden and a largely poor populace is in dire need of new technologies that can rapidly be taken through trials and brought to our patients at affordable costs. This will only be possible if the clinical and scientific community from across diverse fields with an interest in the interplay of immunology and oncology get together and focus their knowledge, skills and energies on this emerging field.

In this context, an interest group formed during the organization of the first Evidence Based Meeting on Immuno-oncology that was held in Tata Memorial Hospital, Mumbai from the 23rd to 25th of February, 2018. The interest group articulated their thoughts and adopted the "Mumbai Resolution" on 24th February 2018, that led to the formation of the Immuno-oncology Society of India (I-OSI) dedicated to the academic pursuit and growth of this field.

The aims of the society, as incorporated in its Constitution, are as follows:

- The society shall be a non-profitable organization for promotion and advancement of scientific knowledge and research in immuno-oncology and increasing the awareness amongst both physicians, scientists, patients and other stakeholders regarding immuno-oncology
- Increase interdisciplinary interactions among all stakeholders dealing with immune-oncology at national and international level
- To encourage basic and clinical research in immuno-oncology and help in translation of laboratory discoveries to patient care
- To assist Government and non-governmental agencies in all matters pertaining to immuno-oncology
- To increase public awareness about immuno-oncology and actively promote continuing education to disseminate the state-of-art knowledge on the basic research and treatment of cancer using immuno-oncology.
- To strive to develop guidelines on development and management of various aspects of immuno-oncology

A list of the executive committee is also displayed in this newsletter and it is obvious that there is adequate representation to all disciplines and all the regions of country to have a true national spirit.

I-OSI will seek to provide a common platform for interaction and mutual collaboration between different specialists and institutes, including industry, sharing a common passion for immuno-oncology. Associations and societies for providing this platform have been constituted in different parts of the world including the Society for Immuno-oncology (SITC) based in North America.

In India, there are a large number of patients, excellent expertise, and perhaps more importantly, a growing recognition of generating world class basic, clinical and epidemiological data and I-OSI hopefully would provide an appropriate forum to talk, deliberate, and execute quality research.

We are beginning to weave with the faith that nature will give the thread and the I-OSI delivers the planned objectives.

Success depends on our perspective and our ingenuity. If we remain open to possibilities and make full use of the resources with each one delivering the best we will achieve our ultimate goal, which goes without saying, is to help our patients and their families.

It takes a whole village to raise a child and I sincerely look forward to your full heart efforts to thoughts and suggestions for the society.

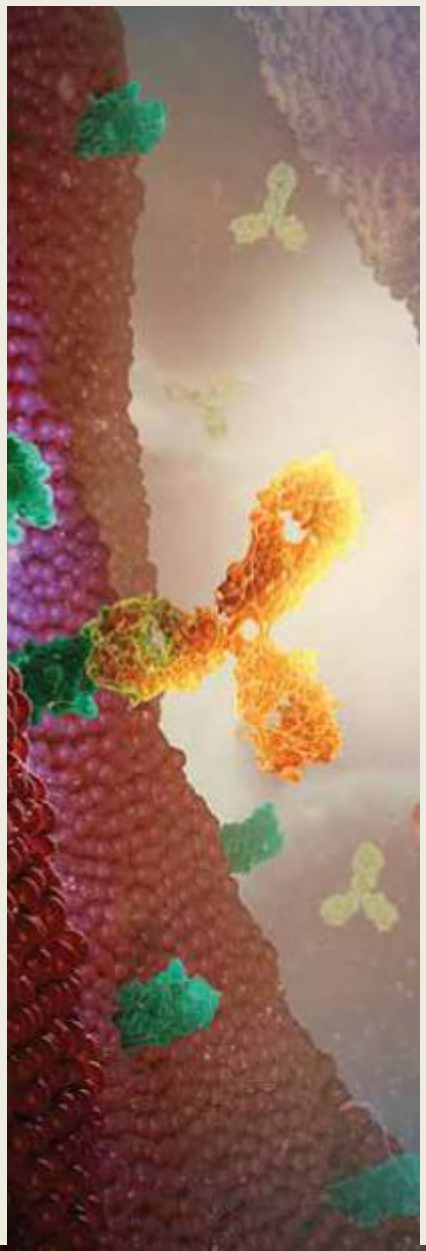
Thank you for your interest and happy reading!

Warm Regards,

Dr. Jyoti Bajpai
General Secretary
Immuno-Oncology Society Of India

Message from I-OSI President Elect

Dr. Hemant Malhotra
President, Indian Society of Medical & Pediatric Oncology (ISMPO) &
Senior Professor, Department of Medicine & Head, Division of Medical Oncology,
RK Birla Cancer Center, SMS Medical College Hospital, Jaipur.



Dear Friends,

Immunotherapy for malignant diseases has been labeled as the 'advance of the decade' and some unbelievable responses in end-stage patients have been recorded. The field has moved from the initial studies on disseminated malignant melanoma to almost all solid tumors and to first line treatment. These advances in solid tumor oncology have been paralleled with the development of CAR T cell therapies for liquid tumours.

The conception of the Immuno-Oncology Society of India (I-OSI) was with the vision, to have a cohesive amalgamation of immunologists and oncologists and the diverse fields whose contributions have resulted in successful development, implementation and assessment of cancer immunotherapy including radiation oncology, pathology, transfusion medicine, surgery and imaging modalities. Real progress can only be made when we have the bench scientists on the same page as the bedside clinicians!

In a country like India, where very few patients are candidates for these very expensive drugs, the need for indigenous research and development of our own immune-therapy molecules and an Indian-Car is the need of the hour. We strongly feel that the Society will promote development, implementation, and dissemination of scientific, evidence-based and comprehensive management of cancers by immunotherapy, and encourage basic and clinical research in the complex interplay of immunology and oncology.

The birth of the Society and the inauguration of the first newsletter is a proud moment for all of us. I encourage all the members to be dedicated to the academic pursuit and growth of this field and the Society to benefit masses of the patients in the country and the community as a whole.

Warm Regards,

Dr. Hemant Malhotra
President Elect
Immuno-Oncology Society Of India

I-OSI Executive Committee Members

The following are the members, their names and addresses, designations, email Id who are the members of the Executive Committee (EC) of the above society. And they are entrusted the work and management of the society as per Rules and Regulations of the society.

President

Dr. Shubhada Chiplunkar

Director, Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Navi Mumbai, Maharashtra

schiplunkar@actrec.gov.in

General Secretary

Dr. Jyoti Bajpai

Professor, Medical Oncology, Tata Memorial Centre, Mumbai, Maharashtra

dr_jyotibajpai@yahoo.co.in

Vice President

Dr. Hemant Malhotra

Professor of Medicine at the SMS Medical College Hospital & Head of the division of Medical Oncology at the Birla Cancer Center, Jaipur Rajasthan

drmalhotrahemant@gmail.com

Joint Secretary

Dr. Vivek Radhakrishhnan

Senior Consultant in Haematology/Oncology and BoneMarrow Transplant - Tata Medical Center, Kolkata, West Bengal

drvivekradhakrishnan@yahoo.com

Treasurer

Dr. (SurgCdr)Gaurav Narula

Professor, Medical Oncology, Tata Memorial Centre, Mumbai, Maharashtra

drgauravnarula@gmail.com

I-OSI Executive Committee Members

Dr. S.D. Banavali

Professor and Head, Medical Oncology, Tata Memorial Centre, Mumbai, Maharashtra

banavali_2000@yahoo.com

Dr. B.K.Smruti

Senior Medical Oncologist and Hemato-Oncologist, Lilavati Hospital and research Centre, Bombay Hospital, Mumbai, Maharashtra

drsmruti20126@gmail.com

Dr. Vikram Mathews

Professor and Head, Christian Medical College & Hospital, Vellore, Tamil Nadu

vikram@tmcvellore.ac.in

Dr. Reena Nair

Senior Consultant, Department of Clinical Hematology, Tata Medical Centre, Kolkata, West Bengal

reenanair@email.com

Dr. Atul Sharma

Professor, Medical Oncology, IRCH, All India Institute of Medical Sciences, New Delhi, India

atul1@hotmail.com

Dr. Rakesh Jalali

Medical Director, Apollo Proton Cancer Centre, Chennai, Tamil Nadu

jalali.rakesh@gmail.com

I-OSI Executive Committee Members

Dr. Kumar Prabhash

Professor, Medical Oncology, Tata Memorial Centre, Mumbai, Maharashtra

kprabhash1@gmail.com

Dr. Senthil Rajappa

Consultant Medical Oncologist, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, Andhra Pradesh

senthiljrajappa@gmail.com

Dr. Moni Abraham Kuriakose

Director, Cochin Cancer Research Centre Govt Medical College Campus Kalamassery, Ernakulam, Kerala

makuriakose@gmail.com

Dr. Amit Awasthi

PhD, Associate Professor, Translational Health Science and Technology Institute (an autonomous institute of Dept. of biotechnology, Govt. of India), Faridabad-Gurgaon, Haryana

awasthi005@gmail.com

Dr. Girdhari Lal

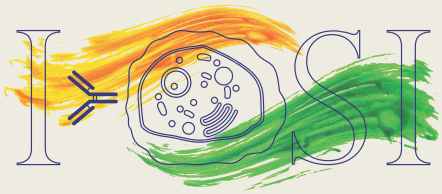
PhD, Scientist 'E', National Centre for Cell Science, Pune, Maharashtra

glal@nccs.res.in

Dr. Rahul Purvar

Assistant Professor IIT-Bombay, Powai, Mumbai, Maharashtra

purwarrahul@iitb.ac.in



IMMUNO-ONCOLOGY SOCIETY OF INDIA

Contact address: 1115, 11th Floor, Homi Bhabha Block, Tata Memorial Centre, Dr. Ernest Borges Road, Parel, Mumbai – 400 012, Maharashtra, India Tel. 022-24177287, Fax: 022-24177287, E-mail: iosi.register@gmail.com

MEMBERSHIP FORM - Fees Rs. 5000/-

Online registration link - https://in.eregnow.com/ticketing/register/I-OSI19

If you are facing any technical issues in online registration then you can make the Demand Drafts or Cheque in favor of " IMMUNO-ONCOLOGY SOCIETY OF INDIA " & Courier it along with the registration form to the above address.

For more information on registration please visit: www.immunooncologyindia.com or write to iosi.register@gmail.com

Title: Prof. ☐ Dr. ☐ Mr. ☐ Mrs. ☐ Ms. ☐

First Name:_____ Last Name:_____ Middle name: _____

Speciality: _____ Highest qualification: _____

Department: _____

Institution: _____

Email: _____
(All correspondence will be by email)

Postal address: _____

Street: _____

City: _____ State: _____

Country: _____ Pin: _____

Contact No.: _____ Fax: _____

I declare that, I am engaged actively in the practice of specialty of Immuno-Oncology in one or more of its fields (Please mention here below, which specific field)

I, the undersigned hereby desire to become a life member of the Immuno-Oncology Society of India and to consent to the bylaws.

Signature: _____ **Date:** _____

FOR I-OSI OFFICE USE ONLY

Enrolled as Life/ Associate/ Honorary/ Corporate/ NGO Member of 'Immuno-Oncology Society of India.'

Name. _____

Folio No. _____

Receipt No. _____ Dated _____

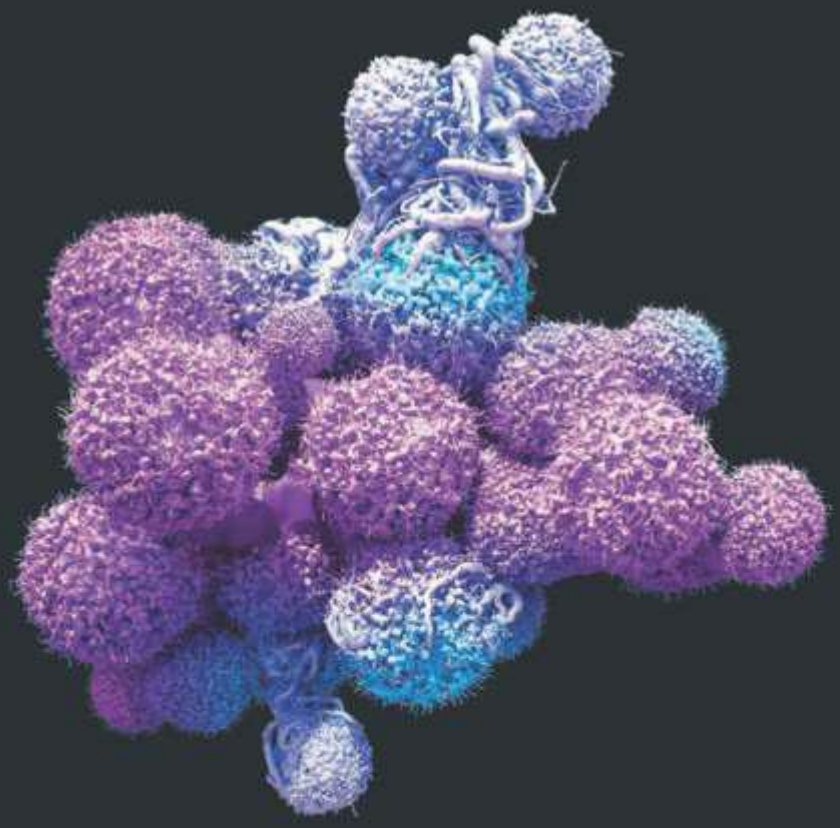
Authorized signatory

SURVEY

Dear Colleagues,

On behalf of the Indian Society Of Immuno-Oncology(I-OSI), I Dr. Jyoti Bajpai, hereby request you to please spare your 5 minutes in responding to this survey questionnaire, which will help us to understand the current practice of Immunotherapeutics usage in the oncology and practical challenges associated with it in the Indian context.

Survey Link: http://rrcgvir.com/iosi/



THERE WERE THOSE WHO BELIEVED
THE BODY COULD NEVER FIGHT CANCER.

NEVER SAY NEVER.

Upcoming Meeting

1st Immuno-Oncology Society of India
Annual Congress 2019
15th-17th MARCH, 2019
Tata Memorial Centre, Mumbai

IMMUNO-ONCOLOGY SOCIETY OF INDIA

Conference theme "Immunotherapies in Cancer: Challenges in translating from bench to bedside"

HIGHLIGHTS OF THE CONGRESS

- Immunomodulatory Antibodies
- Bispecific Antibodies
- Immuno-Oncology Targets
- Combination Immunotherapy
- Preclinical & Translational IO
- Personalized Cancer Vaccines
- IO Biomarkers 1: Immune Profiling and Immune Monitoring
- IO Biomarkers 2: Predictive Biomarkers and Companion Diagnostics
- Neoantigen Targeted Therapies
- Oncolytic Virus Immunotherapy
- Adoptive T Cell Therapy 1: Discovery
- Adoptive T Cell Therapy 1: Development
- Evaluating response in Immunotherapy
- Toxicity management of Immunotherapy drugs
- Stem cell transplant
- Case based panel discussion
- Immuno-Oncology Consensus Guidelines

Dear Colleagues,

It is our pleasure to invite you for the 1st Immuno-Oncology India Congress 2019 (I-OSICON 2019), from **15th-17th March, 2019** at the Tata Memorial Centre (TMC) Mumbai, India, the leading tertiary cancer treatment and research centre in South Asia, one of the largest in the world.

Immuno-Oncology is a rapidly developing field of cancer and causing a paradigm shift in our approach to intractable issues in oncology hitherto. India and the surrounding regions carry a disproportionately large burden of global cancer patients with a fraction of the resources. The emerging promise of immunotherapy will find wide applicability from development to end-use stages.

I-OSICON 2019 will focus on the latest developments and findings in Immuno-Oncology including available treatments, as well as those in the development stage. The congress will welcome all disciplines of Oncology, Immunology, Researchers, Industry leaders, Regulators and Subject-experts.

With the introduction of this congress in Asia region we intend to provide an international platform for discussion of present and future challenges in Immunology education. National and international experts will present cutting-edge and practical clinical techniques based upon widely accepted evidence and will introduce new and emerging research.

This gathering incorporates plenary lectures, keynote speakers, poster/oral presentations, young researcher sessions, symposiums, workshops and exhibitions. It will focus on a wide array of topics including Emerging Immunotherapies, Engineered and Non-engineered Cellular therapies, Evidence-Based Immunotherapy for the Practitioner, Potential Immunological targets, Immune checkpoint inhibitors, Immune Responses and Adverse Events, Response evaluation in Immunotherapy, Precision Genomics and Precision Medicine for Immuno-Oncology, Technological developments of Immuno-Oncology, CAR T-cell production and Regulatory challenges in Immuno-therapies. We plan to have a half day workshop on day 1 followed by the conference for 2 and a half days.

Notably, the conference proceedings and abstracts will be published in the "Journal of Immunotherapy & Precision Oncology ".

We are inviting leading internationally acclaimed researchers, basic scientists and clinicians as faculty and expect a large gathering of attendees. Your participation will be of great encouragement to us and will also add lot of value to the congress in achieving its educational objectives.

Kindly block your dates.

Looking forward to welcoming you for this exciting congress.

Regards,

Organizing Core Committee Members

Patrons
Dr. R. A. Badwe
Dr. S. V. Chiplunkar

Convener
Dr. Hemant Malhotra

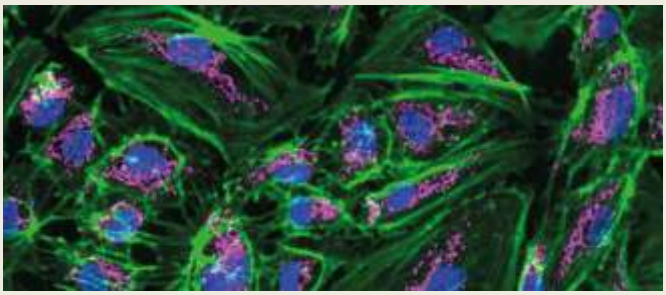
Treasurer
Dr. (SurgCdr) Gaurav Narula

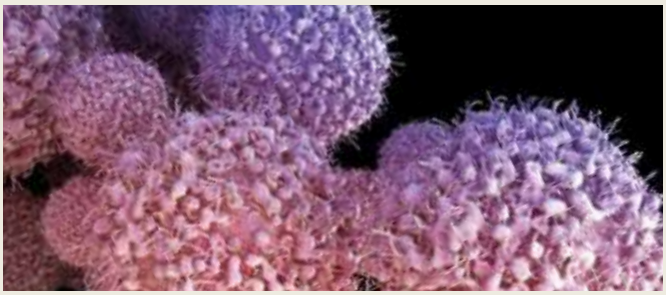
Chairman, Organizing Committee
Dr. S. D. Banavali
Dr. Atul Sharma

Organizing Secretary
Dr. Jyoti Bajpai

Chairman, Scientific Committee
Dr. Rakesh Jalali
Dr. Kumar Prabhash

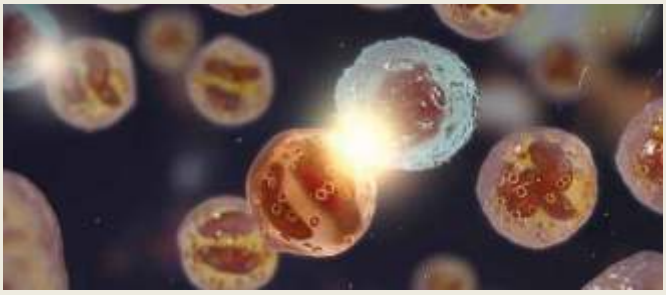
Dr. Anita Ramesh, Chennai
Dr. Asha Kapadia, Mumbai
Dr. Ashish Bakshi, Mumbai
Dr. Ashok Vaid, Delhi
Dr. Bharath Rangarajan, Coimbatore
Dr. Bhavna Parikh, Mumbai





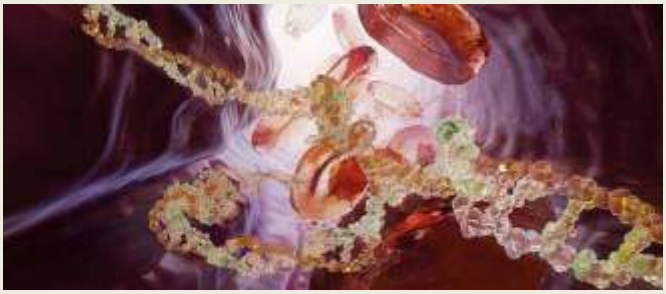
Dr. Biswajit Dubhashi, Pondicherry
Dr. Chetan Deshmukh, Pune
Dr. Chirag Desai, Ahemdabad
Dr. D.C. Doval, Delhi
Dr. G.S. Bhattacharyya, Kolkatta
Dr. Geetha Narayanan, Trivandrum

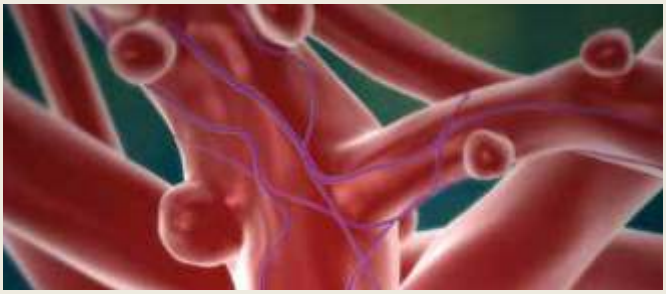
Dr. Girdhari Lal, Pune
Dr. GK Rath, Delhi
Dr. Govind Babu, Bengaluru
Dr. Jaya Ghosh, Mumbai
Dr. Krishna Sainis, Mumbai
Dr. Lalit Kumar, Delhi



Dr. M.B. Agarwal, Mumbai
Dr. Manish Agarwal, Mumbai
Dr. Moni Abraham Kuriakose, Bengaluru
Dr. Navin Khattry, Mumbai
Dr. Poonam Patil, Bangaluru
Dr. Purvish Parikh, Mumbai
Dr. Pankaj Shah, Ahemdabad

Dr. Rajiv Sarin, Mumbai
Dr. Rahul Purwar, Mumbai
Dr. Reena Nair, Kolkatta
Dr. Sadashivudu Gundeti, Hyderabad
Dr. Senthil Rajappa, Hyderabad
Dr. Shyam Agarwal, Mumbai
Dr. Sudeep Gupta, Mumbai





Dr. T Raja, Mumbai
Dr. Tapan Saikia, Mumbai
Dr. Vanita Noronha, Mumbai
Dr. Venkat Radhakrishnan, Chennai
Dr. Vikram Mathews, Vellore
Dr. Vinay Deshmane, Mumbai

International Speakers

Dr. Sanjiv S Agarwala, M.D.
Chief, Medical Oncology & Hematology
St. Luke's University Health Network,
USA

Dr. Naval Daver
Associate Professor, Dept. of Leukemia
MD Anderson Cancer Center,
USA

Dr. Aung Naing, MD, FACP
Associate Professor,
Dept. of Investigational Cancer Therapeutics,
Division of Cancer Medicine,
The University of Texas MD Anderson
Cancer Centre. Houston,
USA

Dr. Herbert Loong
Assist. Professor, Dept. of Clinical Oncology
Deputy Medical Director, Phase 1 Clinical Trials,
The Chinese University of Hong Kong,
Prince of Wales Hospital
Hong Kong

Abstract Submission Regulations and Instructions

Regular Abstract Submission Methods & Deadline - **Tuesday, 15th Jan 2019**

All abstracts for the I-OSICON 2019 must be submitted by the deadline of 21:00 Hrs by **Tuesday 15th Jan 2019**. Abstract submission is free of charge and must be completed online only via the I-OSICON website. Abstracts submitted by e-mail, post or fax will NOT be accepted

Submission Categories

- Biomarker development
- Therapeutic development
- Miscellaneous
- Clinical practice (including toxicities)
- Cell therapy

Type : Randomised, Prospective, Retrospective studies, Case series, Case reports, Intersting reviews on Immuno-oncology reltaed topics.

Please visit our website for submission Instructions (www.immunooncologyindia.com)

SOP For Conducting Pre-conference Workshops

Submitting Application to Conduct Proposed Workshop:

Any oncologist who is a member of either I-OSI or is willing to be a member (submitting application with this request) is eligible to request to conduct a workshop.

A one/ two page executive summary proposal to be forwarded to the organizing committee by email to drjyotibajpai01@gmail.com

Applicants can be from anywhere in the country or outside. However each workshop MUST have a local coordinator from Mumbai.

For complete information on Salient Features and Prerequisites While Planning the Workshop please visit our conference website www.immunooncologyindia.com

1st Immuno-Oncology Society of India Annual Congress 2019
15th-17th MARCH, 2019
Tata Memorial Centre, Mumbai

IMMUNO-ONCOLOGY SOCIETY OF INDIA

REGISTRATION FORM

(Please fill the form in capital letters)

Participants Details:

Full Name: _____

Mobile No: _____ Email Id: _____

Institution: _____

Department: _____ Specialization: _____

Postal Address: _____

_____

City: _____ State: _____

Payment Details: _____

Amount: _____

DD/Cheque No: _____

Bank Name: _____

Conference Registration Fees

Delegates	Rs. 5000/-	Membership + Delegates	Rs. 8000/-
Students	Rs. 3000/-	Membership + Student	Rs. 6000/-

Only Membership Fee: Rs.5000/-

Online registration link - https://in.eregnow.com/ticketing/register/I-OSI19

If you are facing any technical issues in online registration then you can make the Demand Drafts or Cheque in favor of " IMMUNO-ONCOLOGY SOCIETY OF INDIA " & Courier it along with the registration form to the below address of conference secretariat.

For more information on registration please visit www.immunooncologyindia.com or write to iosi.register@gmail.com

Conference Secretariat :

River Route® Events

ADITI MISTRY
RIVER ROUTE CREATIVE GROUP LLP
Unit No. 9, Ground Floor, Cama Industrial Premises Co-Op Society Ltd
Sunmill Compound, Lower Parel(W), Mumbai, Maharashtra 400 013
Tel: 022 24931358/59, Mob: +91 70215 69423 Email: iosi.register@gmail.com

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO IMMUNO-ONCOLOGY CONGRESS

GENEVA SWITZERLAND
13-16 DECEMBER 2018

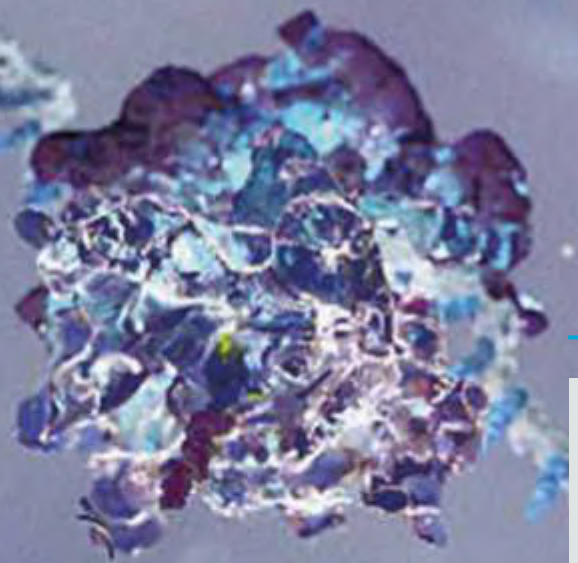
ASCO-SITC

Clinical Immuno-Oncology Symposium

February 28-March 2, 2019

San Francisco Marriott Maruuis | San Francisco, CA

#ImmunoOnc19



Immuno-Oncology websites

www.immuno-oncologysummit.com
www.immuno-oncology2019.com
www.immuno-oncology.euroscicon.com
www.immunosym.org
www.immuno-oncologyeurope.com
www.sitcancer.org

Inspiring Great Scientists

James Allison, USA Tasuku Honjo, Japan

Immunologists Win Nobel Prize in Medicine for Groundbreaking Cancer Research

Two immunologists, James Allison of the United States and Tasuku Honjo of Japan, have won the 2018 Nobel Prize in Medicine.

Allison and Honjo will share the Nobel Prize sum of nine million Swedish kronor (about $1 million or €870,000).

The award recognizes their research on two different checkpoint inhibitor molecules — the "brakes" of our immune system — that when turned off, boost the body's immune response against cancer cells faster and more effectively.

Conventional chemotherapy attempts to target and destroy cancer cells, but it also destroys healthy cells, causing a series of adverse side effects. Allison, 70, and Honjo, 76, brought forward the benefits of targeted cancer immunotherapy, which uses the power of the body's own immune system to fight cancer cells, while leaving healthy cells unharmed.

Back in 1995, Allison was one of two researchers who discovered one of these immune system brakes, called CTLA-4. This is an inhibitory receptor found on the surface of T-cells — the killers of our immune system. Shortly after, Allison realized the true therapeutic potential of his discovery: remove the brake to drive immune cells to attack tumors directly.

Around the same time, Honjo found another molecule in immune cells, the PD-1 receptor, which also acted as a brake, but in a different way.

Normally, when the receptor, found on T-cells, interacts with its ligand, which is produced by healthy cells, it basically tells the T-cell to leave the other cell alone. However, some cancer cells hijack this mechanism to evade being detected and killed by T-cells.

Since its discovery, several antibodies against the PD-1 receptor, including Opdivo (nivolumab), Keytruda (pembrolizumab) and Tecentriq (atezolizumab), have won U.S. Food and Administration (FDA) approval.

Keytruda became even more famous after it helped former President Jimmy Carter survive advanced-stage melanoma (skin cancer) that had already spread to his brain.

Meanwhile, Allison's research led to the development of Yervoy, a monoclonal antibody targeting CTLA-4 that was approved by the FDA in 2011 to treat melanoma.

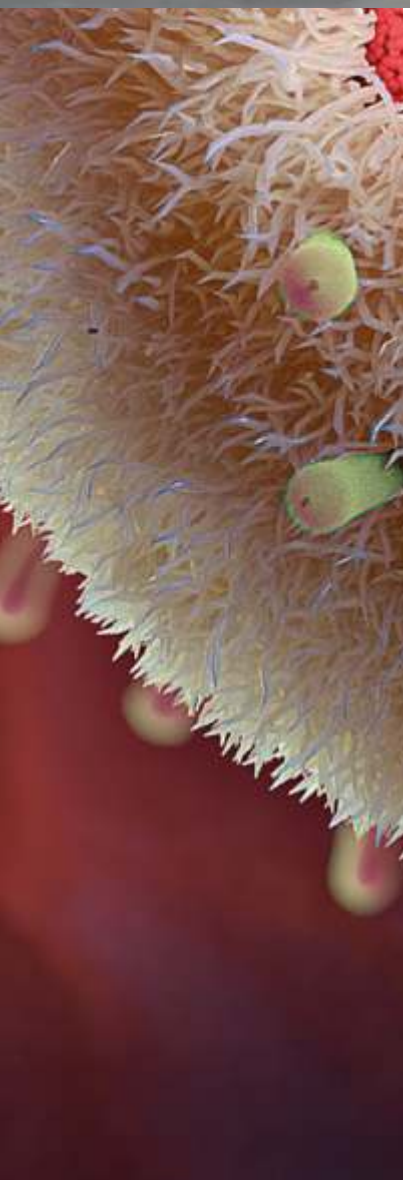
"I never dreamed my research would take the direction it has," Allison said in a press release. "It's a great, emotional privilege to meet cancer patients who've been successfully treated with immune checkpoint blockade. They are living proof of the power of basic science, of following our urge to learn and to understand how things work."

Honjo also said he wants to continue his research in immunotherapy, in order to save as many cancer patients as possible.

The Nobel Assembly stressed the importance of developing new therapeutic strategies against cancer, now the world's second largest cause of death.

India can

"Indigenous CAR-T Cell Technology on the Indian Clinical Horizon"



CAR-T cell therapy has demonstrated remarkable success in long-term remission of relapsed or refractory B-ALL (r/r B-ALL). Recently, FDA approved the clinical use of CAR-T cells for few CD19 + malignancies in patients who had second relapse after allogeneic stem cell transplant (allo-SCT). Given majority of patients in India are unable to afford allo-SCT, the potential clinical use of CAR T cells as a first line therapy for r/r B-ALL remains unknown.

Dr. Rahul Purwar at IIT Bombay, as a first step, a novel humanized anti-CD19 CAR construct was designed and CD19-vector was produced using 3rd generation lentiviral mediated gene delivery system. Efficacy and safety profile of CD19+CAR T cells from healthy subjects were tested. The comprehensive data shows that they have successfully designed, developed and tested the efficacy and safety profile of indigenous humanized CD19 + CAR-T cells in ex vivo settings. Next step is to validate these results with patient samples and develop a CAR-T cell manufacturing process as per industry standards with an ultimate goal of first-in-human clinical trial at Tata Memorial Center Mumbai and Dr. Norula is working with Dr. Purwar in this project.

Amit Awasthi, Associate Professor, The Translational Health Science and Technology Institute is leading the research in the area of understanding the interplay between effector and regulatory T cells in IBD. Understanding T cell differentiation pathways in immunity, autoimmunity and cancer immunity. One of major interest of their lab is to identify the mechanisms and metabolic regulation of anti-tumour T cells as well as identify small molecules to target check point inhibitors in cancer immunotherapy.

Approved Indication for Immuno-Oncology Products

NIVOLUMAB Indications

It is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of

- Patients with BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent.
- Patients with BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent.
- Patients with unresectable or metastatic melanoma, in combination with ipilimumab.
- Patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting.
- Patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy.
- Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.
- Patients with metastatic small cell lung cancer with progression after platinum based chemotherapy and at least one other line of therapy.
- Patients with advanced renal cell carcinoma who have received prior antiangiogenic therapy.
- Patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab.
- Adult patients with classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximabvedotin, or 3 or more lines of systemic therapy that includes autologous HSCT.
- Patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy.
- Patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy
- Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- Adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab.
- Patients with hepatocellular carcinoma who have been previously treated with sorafenib.b (1.10) a This indication is approved under accelerated approval based on progression-free survival.

Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

PEMBROLIZUMAB Indications

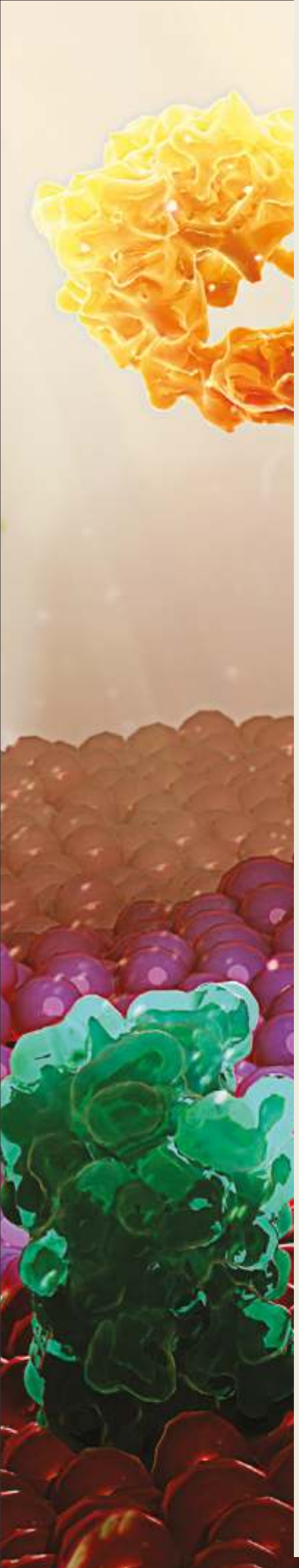
PEMBROLIZUMAB is a programmed death receptor-1 (PD-1)-blocking antibody indicated in

Melanoma

- For the treatment of patients with unresectable or metastatic melanoma.

Non-Small Cell Lung Cancer (NSCLC)

- In combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumor aberrations.



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- As a single agent for the first-line treatment of patients with metastatic NSCLC whose tumors have high PD-L1 expression [(Tumor Proportion Score (TPS) ≥50%)] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
- As a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

Head and Neck Squamous Cell Cancer (HNSCC)

- For the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

Classical Hodgkin Lymphoma (cHL)

- For the treatment of adult and pediatric patients with refractory cHL, or who have relapsed after 3 or more prior lines of therapy.

Primary Mediastinal Large B-Cell Lymphoma (PMBCL)

- For the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy.

Urothelial Carcinoma

- For the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA-approved test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.
- For the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Microsatellite Instability-High Cancer

- For the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient
  - solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
  - colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- Limitation of Use: The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

Gastric Cancer

- For the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.

Cervical Cancer

- For the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA approved test.

Approved Indication for Immuno-Oncology Products

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

DURVALUMAB Indication

DURVALUMAB is a programmed death-ligand 1 (PD-L1) blocking antibody indicated for the treatment of patients with, Locally advanced or metastatic urothelial carcinoma who:

- have disease progression during or following platinum-containing chemotherapy
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy

ATEZOLIZUMAB indication

ATEZOLIZUMAB is a programmed death-ligand 1 (PD-L1) blocking antibody indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are

- Not eligible for cisplatin-containing chemotherapy, and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 5% of the tumor area),
- or are not eligible for any platinum-containing chemotherapy regardless of level of tumor PD-L1 expression,
- or have disease progression during or following any platinum-containing chemotherapy,
- or within 12 months of neoadjuvant or adjuvant chemotherapy.

This indication is approved under accelerated approval based on tumour response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Metastatic non-small cell lung cancer who have disease progression during or following platinum- containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA approved therapy for these aberrations prior to receiving ATEZOLIZUMAB.

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Immunotherapy- A Future of Cancer Management

Pioneering work has unraveled the role of the immune system in the development and control of cancer. This knowledge has set the basis for the successful implementation of immunotherapy into the standard of care for a large number of cancer types. Based on response rates and prolongation of overall survival, immunotherapeutic approaches have been approved in a growing number of tumor diseases. Activation or therapeutic utilization of T cells represent the basis of these concepts. Checkpoint inhibitory antibodies inhibiting CTLA-4, PD1 and PD-L1 receptors and ligands induce long-term clinical tumor control in a significant number of cancer patients including metastatic melanoma and non-small cell lung cancer.

Highlights from ESMO 2018

Atezolizumab (Tecentriq), combination shows statistically significant improvement in both progression-free and overall survival (OS) in NSCLC

ESMO 2018,Abstract LBA53., Cappuzzo F

"The IMpower130 results support atezolizumab plus chemotherapy as a treatment option for patients with advanced nonsquamous NSCLC, irrespective of PD-L1 status," said Federico Cappuzzo, MD, director of medical oncology and of the Department of Hematology and Oncology at the Azienda Unità Sanitaria Locale della Romagna-Ravenna in Italy.

Impower130 is a multicenter, open-label, randomized phase III study investigating atezolizumab plus carboplatin/ nabpaclitaxel compared with carboplatin/ nab-paclitaxel alone in chemotherapy-naïve patients with stage IV nonsquamous NSCLC with measurable disease.

There were 723 patients in the intent-to-treat (ITT) population and 679 patients in the ITT–wild-type (WT) population, which excluded patients with EGFR/ALK abnormalities. The co-primary endpoints were investigator-assessed PFS and OS in the ITT-WT cohort; secondary endpoints were OS and PFS in the ITT group, as well as PD-L1 expression, ORR, and safety.

Results showed that, in the ITT-WT population, the median PFS with the atezolizumab regimen was 7.0 months (95% CI, 6.2-7.3) and 5.5 months (95% CI, 4.4-5.9) for carboplatin/nab-paclitaxel alone (HR, 0.64; 95% CI, 0.54-0.77; P <.0001). The 6- and 12-month PFS rates also favored the atezolizumab arm at 56.1% and 29.1% versus 42.5% and 14.1% with chemotherapy.

The atezolizumab arm was also superior in OS in the ITT-WT population, with a median of 18.6 months (95% CI, 16.0-21.2) versus 13.9 months (95% CI, 12.0-18.7) with carboplatin/nab-paclitaxel alone (HR, 0.79; 95% CI, 0.64-0.98; P = .033). The 1- and 2-year OS rates with atezolizumab were 63.1% and 39.6% versus 55.5% and 30.0% in the carboplatin/nab-paclitaxel arm.

ORR and median DOR was 49.2% and 8.4 months (6.9-11.8) with the atezolizumab regimen versus 31.9% and 6.1 months (5.5-7.9) with chemotherapy (P = .0004). In the atezolizumab arm, the ORR consisted of a 2.5% complete response rate, 46.8% partial response rate, 30.4% stable disease rate, and 11% progressive disease rate. Responses were ongoing in 36.8% of patients on atezolizumab and 19.4% on chemotherapy.

The PFS benefit was observed across all prespecified subgroups, except for those with liver metastases (HR, 0.93; 95% CI, 0.59-1.47); this group also did not experience an OS benefit (HR, 1.04; 95% CI, 0.63-1.72).

Investigator-assessed PFS and OSS in the ITT population were similar to the ITT-WT population, with a median PFS of 7.0 months for atezolizumab and 5.6 months

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for carboplatin/nab-paclitaxel (HR, 0.65; 95% CI, 0.54-0.77; P <.0001). The 6- and 12-month PFS rates were 56.4% and 28.9% with atezolizumab and 42.9% and 14.2% for chemotherapy.

The median OS for the ITT group for atezolizumab and chemotherapy was 18.1 months and 13.9 months, respectively (HR, 0.80; 95% CI, 0.65-0.99; P = .039). Additionally, the 1- and 2-year OS rates in this group were 62.7% and 39.3% on the atezolizumab arm and 55.1% and 29.9% with carboplatin/nab-paclitaxel.

The PFS and OS benefits varied in the EGFR/ALK-positive subgroups; the median PFS was 7.0 months and 6.0 months with atezolizumab and carboplatin/nab-paclitaxel alone (HR, 0.75; 95% CI 0.36-1.54), respectively; median OS was 14.4 months and 10.0 months (HR, 0.98; 95% CI, 0.41-2.31).

PFS data were also reported by levels of high, low, and negative PD-L1 expression: high (6.4 vs 4.6 months; HR, 0.51; 95% CI, 0.34-0.77), low (8.3 vs 6.0 months; HR, 0.61; 95% CI, 0.43-0.85), and negative (6.2 vs 4.7 months; HR, 0.72; 0.56-0.91). For OS, the benefit was similar: high (17.3 vs 16.9 months; HR, 0.84; 95% CI, 0.51-1.39), low (23.7 vs 15.9 months; HR, 0.70; 95% CI, 0.45-1.08) and negative (15.2 vs 12.0 months; HR, 0.81; 95% CI, 0.61-1.08).

In the ITT-WT population, 39% of patients on the atezolizumab arm received subsequent therapy compared with 66.2% on carboplatin/paclitaxel; moreover, 40.8% of patients on chemotherapy crossed over to receive atezolizumab.

Opdivo-Yervoy Combo Shows Potential as First-line Treatment for Certain Colorectal cancers

ESMO 2018, Abstract LBA18_PR., Heinz-Josef Lenz

A combination of Opdivo (nivolumab) and low-dose Yervoy (ipilimumab) induced promising and durable response rates in metastatic colorectal cancer patients with certain genetic abnormalities who had not received prior treatments, Phase 2 data shows.

These findings suggest the combination may become the next first-line therapy for metastatic colorectal cancer patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumours.

Tumors with MSI-H and dMMR are those with mutations in genes that normally repair DNA. These patients are usually less responsive to chemotherapy and show shorter survival times.However, the accumulation of mutations in tumor cells with these deficiencies sometimes generate structurally different proteins that the immune system identifies as malignant, making these tumours more responsive to immunotherapies.

Results from the CheckMate-142 study had already shown that a combination of Opdivo and low-dose Yervoy induced high and durable response rates in MSI-H metastatic colorectal cancer patients who had failed prior chemotherapy. The findings led to an accelerated approval from the U.S. Food and Drug Administration earlier this year.

Researchers are now reporting data from patients who had not yet received treatment for their MSI-H/dMMR metastatic colorectal cancers.

The study included 45 patients (51% men, median age of 66 years), who received Opdivo every two weeks and low-dose Yervoy every six weeks until their disease progressed or they experienced any signs of toxicity. Its main goal was overall response rate.

After a median follow-up of 13.8 months, the combination had partially shrunk the tumors of 53% patients and completely eliminated traces of tumor in 7%.

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Additionally, 23% of patients achieved disease stabilization with the treatment, amounting to a total disease control rate of 83%.

At the time of the analysis, more than half of patients were still responding to the combination. After one year, 83% of patients remained alive, and 77% were alive and disease-free.

While other trials had tested a combination of Opdivo and Yervoy, the use of low-dose Yervoy in the CheckMate-142 study resulted in fewer side effects. Severe or life-threatening adverse events were reported by 16% of patients, with only 7% of participants discontinuing treatment due to treatment-related adverse events.

Keytruda Improves Survival in Patients with Relapsed or Metastatic Head, Neck Cancer, Interim Data Show

ESMO 2018, Abstract LBA8_PR.,Barbara Burtness

First-line treatment with Keytruda (pembrolizumab) — alone or in combination with standardchemotherapy — significantly prolongs survival of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), compared to standard treatment, according to interim results of a Phase 3 clinical trial.

The randomized, open-label, Phase 3 trial (NCT02358031), also known as KEYNOTE-048, is evaluating Keytruda — alone or in combination with standard chemotherapy (platinum-based and Adrucil chemotherapy) — as a first-line treatment in patients with head and neck squamous cancer that has relapsed or spread to other parts of the body.

The trial's primary goals are overall survival and progression-free survival (PFS), or the time a patient lives without cancer progression, in patients whose tumors produce PD-L1 and in all patients regardless of PD-L1 presence.
PD-L1 presence was measured by a combined positive score (CPS), which includes levels of PD-L1 on both the tumor and surrounding cells. Patients with positive detection of PD-L1 were divided into two CPS categories: equal or above 20 (high levels), and equal or above one (low levels).

The trial's secondary goals include treatment response rate and global health status or quality of life.

KEYNOTE-048 enrolled 882 patients with head and neck squamous cancer who had not received prior systemic therapy for relapsed or metastatic disease. Patients were randomized to receive either Keytruda alone (300 patients), Keytruda in combination with standard chemotherapy (281 patients), or standard therapy (300 patients), for up to two years.

Barbara Burtness, the study's first-author and co-director of the Development Therapeutics Research Program, at Yale Cancer Center, presented the KEYNOTE-048 results collected until June 13, 2018, with a minimum follow-up of about 17 months.

Keytruda alone significantly prolonged the survival of patients with high (14.9 months) or low (12.3 months) levels of PD-L1, compared to standard treatment (10.3 and 10.7 months, respectively).

While fewer patients responded to Keytruda (17%) than to standard therapy (36%), the median duration of treatment response was longer in the Keytruda group (20.9 months), compared to that of the standard treatment group (4.5 months).

The combination of Keytruda and standard chemotherapy also significantly extended the patients' survival (13.0 months), compared to standard care (10.7 months). Among patients producing high or low levels of PD-L1, no differences in overall survival were found between both

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treatment groups.
Treatment response rates were similar between patients receiving the combo therapy (35.6%) and those receiving standard care (36.3%), but the response duration also was prolonged in the combo therapy group.

The results also showed that Keytruda alone or combined with standard chemotherapy did not prolong patients' PFS, compared with standard treatment.

The safety profiles of the three treatment regimens were consistent with those reported in previous clinical studies. Keytruda alone was less toxic than standard treatment, while Keytruda combined with chemotherapy showed similar toxicity to standard treatment.

The researchers noted that these interim data support Keytruda alone or in combination with standard chemotherapy as new-first line treatments for recurrent or metastatic head and neck squamous cancer.

Imfinzi Prolongs Overall Survival in Advanced NSCLC Patients, Phase 3 Trial Data Show

ESMO 2018,Abstract 1363O.,Faivre-Finn, C

Treatment with Imfinzi (durvalumab) significantly prolongs overall survival among patients with stage III, inoperable non-small-cell lung cancer (NSCLC) in comparison to those given a placebo, according to new data from a Phase 3 clinical trial.

The updated results from the PACIFIC trial (NCT02125461) were presented by AstraZeneca and its global biologics research and development arm, MedImmune, at the recent IASLC 19th World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer in Toronto.

Findings of the study, "Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC," were also published in the New England Journal of Medicine.

Previous data from the PACIFIC trial had demonstrated that Imfinzi significantly extended the time to disease progression or death among patients whose disease did not progress after platinum-based chemotherapy and radiation therapy.

The newly released data, from a subsequent independent interim analysis, revealed that Imfinzi significantly increased overall survival — another primary trial goal — reducing the risk of death by 32% over two years among treated patients. (Median follow-up for overall survival was 25.2 months, the study noted.)

"The five-year survival rate in this setting has historically been around 15% after concurrent chemoradiation therapy. The significant survival benefit observed using the PACIFIC regimen [32%] provides confidence and clear rationale for a new standard of care," Scott J. Antonia, MD, PhD, chair of the Thoracic Oncology Department at Moffitt Cancer Center in Tampa, Florida, and principal investigator for the PACIFIC trial, said in a press release.

Updated trial findings were also consistent with what had been previously reported regarding the safety and tolerability of Imfinzi.

"Updated analyses regarding progression-free survival were similar to those previously reported, with a median duration of 17.2 months in the durvalumab group and 5.6 months in the placebo group. The median time to death or distant metastasis was 28.3 months in the durvalumab group and 16.2 months in the placebo group," the researchers wrote.

Although Imfinzi can lead to serious, sometimes fatal, side effects, most adverse reactions reported in this analysis

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of treated patients compared to placebo were cough (35.2% vs. 25.2%), fatigue (24.0% vs. 20.5%), shortness of breath (22.3% vs. 23.9%) and radiation pneumonitis (a type of lung injury linked to repeat radiation treatment; 20.2% vs. 15.8%).

But the percentage of Imfinzi-treated patients experiencing grade 3 or 4 adverse events was higher than those given a placebo (30.5% vs. 26.1%). More of these patients also stopped treatment due to side effects than did those on placebo (15.4% vs. 9.8%).

Some patients with metastatic triple negative breast cancer live longer with immunotherapy

ESMO 2018,Abstract LBA1_PR., Peter Schmid

The phase III IMpassion 130 trial enrolled 902 patients with metastatic triple negative breast cancer who had not received prior treatment for metastatic disease. Patients were randomly allocated to standard chemotherapy (nab-paclitaxel) plus atezolizumab, an antibody targeting the protein PD-L1, or to standard chemotherapy plus placebo. The two main objectives were to see whether the drug combination could slow cancer growth (progression-free survival) and prolong life (overall survival) in all patients and in those expressing PD-L1. The median follow-up was 12.9 months.

The combination therapy reduced the risk of disease worsening or death by 20% in all patients and 38% in the subgroup expressing PD-L1. In the entire study population, the median progression free survival was 7.2 months with the combination and 5.5 months with chemotherapy alone, with a hazard ratio (HR) of 0.80 (p=0.0025). In the PD-L1 positive group, the median progression free survival was 7.5 months with the combination and 5.0 months with chemotherapy alone (HR 0.62, p<0.0001).

More than half of patients were alive at the time of analysis, so this was an interim assessment of overall survival. In patients with PD-L1 positive tumours, the median overall survival was 25.0 months with the combination compared to 15.5 months with standard chemotherapy alone (HR 0.62). In all patients, survival was 21.3 months with the combination versus 17.6 months with chemotherapy alone which was not statistically different, likely because of the short follow-up.

The proportion of patients responding to treatment (objective response rate) was higher with the combination compared to chemotherapy alone for all patients (56% versus 46%) and those with PD-L1 positive tumours (59% versus 43%).

This combination therapy was well tolerated. Most side effects were due to chemotherapy and occurred at a similar rate in both treatment groups, although there was a minor increase in nausea and cough in the combination group. Side effects related to immune therapy were rare, the most common being hypothyroidism which occurred in 17.3% of patients receiving the drug combination and 4.3% receiving chemotherapy alone.

JAVELIN Renal 101: Avelumab Plus Axitinib in Previously Untreated Renal Cell Carcinoma

ESMO 2018,Abstract LBA6_PR.,Robert Motzer

"JAVELIN Renal 101 is the first positive phase III study combining an immune checkpoint blocker with a tyrosine kinase inhibitor compared to tyrosine kinase inhibitor [treatment] alone in the first-line treatment of advanced RCC," remarked lead author Robert Motzer, MD, of Memorial Sloan Kettering Cancer Center, in a statement. "The findings support the potential of avelumab plus axitinib as a new treatment approach for patients with advanced RCC. The combination benefit was shown in all subgroups of patients, by independent review as well as by investigators, and whether tumor cells stained positive for programmed cell death ligand 1 (PD-L1) or not," he continued.

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"Tyrosine kinase inhibitors [like axitinib] and checkpoint blockers like avelumab both may have potential immune-modulating functions that, when combined, may provide clinical benefit in patients with advanced RCC that exceeds the effects of the respective drugs alone, without compromising toxicity," said Dr. Motzer.

In the global, randomized JAVELIN Renal 101 trial, 886 patients with kidney cancer with all MSKCC (Memorial Sloan Kettering Cancer Center/Motzer score used for selection of patients with metastatic RCC for trial inclusion) prognostic subgroups (good, intermediate, and poor risk) were enrolled and were administered therapy as first-line treatment.

Avelumab was administered to 442 patients at 10 mg/kg intravenously every 2 weeks in combination with axitinib 5 mg orally twice daily. The comparator group of 444 patients received sunitinib (Sutent) given at 50 mg orally once a day on a schedule of 4 weeks on followed by 2 weeks off. The primary outcomes were PFS in patients testing positive for PD-L1 expression patients (up to 30 months); and overall survival in PD-L1–positive patients up to 5 years.

Median PFS was 13.8 vs 7.2 months in the combination arm compared to the sunitinib arm (hazard ratio [HR] = 0.61; P < .0001) in the patients with PD-L1–positive tumors, while median PFS in patients irrespective of PD-L1 expression was 13.8 vs 8.4 months (HR = 0.69; P = .0001) respectively. Confirmed objective response rate was 55.2% (95% confidence interval [CI] = 49.9–61.2) and 25.5% (95% CI = 20.6–30.9), respectively.

Treatment-emergent adverse events of grade 3 and over were experienced by 71.2% vs 71.5% of patients in the combination arm vs the sunitinib arm, respectively, and led to discontinuation of drug in 22.8% vs 13.4%, respectively.

2018 ASCO highlights

KEYNOTE-042 Trial Compares Pembrolizumab With Chemotherapy as First-Line Treatment of NSCLC With PD-L1 Expression of 1% or More

ASCO 2018, Abstract LBA4., Gilberto Lopes

Researchers randomly assigned 1,274 people with locally advanced or metastatic NSCLC to receive chemotherapy (paclitaxel plus carboplatin or pemetrexed plus carboplatin) or pembrolizumab. Both squamous and nonsquamous cancers were included, but cancers with genetic changes that can be treated with targeted therapies (EGFR and ALK inhibitors) were not.

For the analysis, researchers explored treatment benefits in 3 patient groups according to tumor PD-L1 expression score: at least 50% (599 patients), at least 20% (818 patients), and at least 1% (1,274 patients). Equal numbers of patients in each PD-L1 expression group received pembrolizumab and chemotherapy.

Key Findings

The median follow-up time was 12.8 months. Compared with those receiving standard chemotherapy, patients who received pembrolizumab had a longer median overall survival, regardless of PD-L1 expression in the tumor. The benefit of pembrolizumab was greater when the level of PD-L1 expression was higher:

- PD-L1 50% or more: 20 months with pembrolizumab vs 12.2 months with chemotherapy
- PD-L1 20% or more: 17.7 months with pembrolizumab vs 13 months with chemotherapy
- PD-L1 1% or more: 16.7 months with pembrolizumab vs 12.1 months with chemotherapy

IMpower 131 Studies Addition of Atezolizumab to Chemotherapy in Advanced Squamous NSCLC

ASCO 2018,Abstract LBA9000.,Robert M. Jotte

International conference Highlights in Immuno-Oncology

The IMpower131 trial enrolled 1,021 patients with stage IV squamous NSCLC. Tumors were tested for PD-L1 expression, but patients were included in the trial regardless of tumor PD-L1 expression level. Patients with EGFR or ALK gene changes in the tumor received targeted treatments before starting therapy on this trial.

The study participants were randomly assigned to one of three treatment groups. Outcomes for only two of the groups, however, are being reported in this presentation: atezolizumab plus chemotherapy (carboplatin and nab-paclitaxel [Abraxane]), 343 patients; and chemotherapy (carboplatin and nab-paclitaxel), 340 patients. Outcomes data for the third treatment group, which received atezolizumab with a slightly different chemotherapy regimen (carboplatin and paclitaxel), are not yet available.

Key Findings

In this study, 29% of all patients, regardless of PD-L1 expression, had a reduced risk of disease worsening or death, compared with those who received chemotherapy alone. Importantly, there was a doubling of progression-free survival benefit with this combination: At 12 months, cancer had not worsened in 24.7% patients receiving immunotherapy and chemotherapy, compared to 12% of those receiving chemotherapy alone.

Improved progression-free survival was observed in all groups of patients who received immunotherapy and chemotherapy, including those with PD-L1–negative tumors and liver metastases. Overall survival data are not yet mature.

This is the first phase III trial of an immunotherapy-based combined-modality treatment to show a significant improvement in progression-free survival in advanced squamous NSCLC, according to the authors. Although the difference between treatment groups is modest, a statistically significant improvement shows that, overall, people with advanced squamous lung cancer can benefit when immunotherapy is added to standard treatment, according to the authors.

Although the rate of severe side effects was higher with the combined-modality treatment than with chemotherapy alone (68% vs 57%), it had a manageable safety profile, consistent with known safety risks of the individual therapies. The most common side effects of atezolizumab included skin rash, colitis, and low thyroid hormone levels.

At this interim analysis a statistically significant overall survival benefit was not observed (median overall survival was 14 months for atezolizumab plus chemotherapy vs 13.9 months for chemotherapy alone). Researchers are continuing to follow patients and anticipate a subsequent analysis later this year.

Pembrolizumab Plus Chemotherapy as First-Line Treatment of Metastatic Squamous NSCLC: KEYNOTE-407 Study

ASCO 2018,Abstract 105.,Luis Paz-Ares

KEYNOTE-407 is investigating pembrolizumab in combination with carboplatin/paclitaxel or carboplatin/nab-paclitaxel, compared with carboplatin/paclitaxel or carboplatin/nab-paclitaxel alone, in 559 patients with metastatic squamous NSCLC. Patients had not previously received systemic therapy for advanced disease. The dual primary endpoints are overall and progression-free survival, and secondary endpoints include objective response rate and duration of response.

In this study, the median overall survival was 15.9 months in the pembrolizumab combination group (95% CI = 13.2–not estimable) and 11.3 months in the chemotherapy-alone group (95% CI, 9.5–14.8). Of the 42.8% of patients (n = 89) randomly assigned to the chemotherapy-alone group who discontinued chemotherapy went on to receive subsequent anti–PD-1 or anti–PD-L1 therapy, 75 patients received pembrolizumab monotherapy as part of in-study crossover.

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In addition to subgroups based on PD-L1 expression levels, improvements in overall survival were observed in all other patient subgroups evaluated, including age, sex, EGOG performance status score, region of enrollment, and type of taxane prescribed (ie, paclitaxel or nab-paclitaxel). The median progression-free survival was 6.4 months for the pembrolizumab combination (95% CI = 6.2–8.3) compared with 4.8 months for chemotherapy alone (95% CI = 4.3–5.7).

As previously announced, at the first interim analysis, pembrolizumab plus carboplatin and paclitaxel or nab-paclitaxel showed an overall response rate of 58.4% (95% CI = 48.2%–68.1%) compared to 35.0% (95% CI = 25.8%–45.0%) for chemotherapy alone (P = .0004). At the time of the second interim analysis, which also included the survival results announced at the 2018 ASCO Annual Meeting, the overall response rate data were similar to the first, alpha-controlled response rate analysis, as follows: 57.9% (95% CI = 51.9%–63.8%) for the pembrolizumab combination group compared to 38.4% (95% CI = 32.7%–44.4%) for the chemotherapy group. Among patients in the pembrolizumab combination group, the median duration of response was 7.7 months (range = 1.1+ to 14.7+ months) compared with 4.8 months in the chemotherapy alone group (range = 1.3+ to 15.8+ months).

More Evidence of Benefit With Immunotherapy and Chemotherapy in Nonsquamous Non–Small Cell Lung Cancer

ASCO 2018,Abstract 9002., Mark A. Socinski

ATEZOLIZUMAB (TECENTRIQ) plus bevacizumab (Avastin) plus a platinum doublet (ABCP) improved overall survival by 22% compared with bevacizumab plus a platinum doublet (BCP) in patients with advanced wild-type (without an identified mutation) nonsquamous non–small cell lung cancer (NSCLC), according to the results of the phase III IMpower 150 trial presented at the 2018 ASCO Annual Meeting.1Interestingly, survival was also improved by the checkpoint inhibitor/vascular endothelial growth factor (VEGF) inhibitor/chemotherapy combination in patients with epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutations, as well as in those with liver metastasis. Survival improvement was seen with the four-drug combination irrespective of the programmed cell death ligand 1 (PD-L1) expression level. These study findings were published in The New England Journal of Medicine to coincide with the presentation at the ASCO meeting.[2]

The median overall survival was 19.2 months for ABCP vs 14.7 months with BCP (P = .0164). The rate of 24-month overall survival was 43% compared with 34%, respectively. The median progression-free survival was also improved by 1.5 months with the four-drug regimen compared with the three-drug regimen: 8.3 months vs 6.98 months, respectively (P < .0001).

These findings represent more evidence of benefit for checkpoint inhibitor/chemotherapy combinations in nonsquamous NSCLC. The phase III KEYNOTE-189 study showed a similar survival benefit for the combination of pembrolizumab (Keytruda) plus chemotherapy in nonsquamous NSCLC.

"The IMpower150 trial met its co-primary endpoints of progression-free and overall survival and demonstrated a statistically significant and clinically meaningful benefit with atezolizumab plus bevacizumab and chemotherapy vs bevacizumab plus chemotherapy alone in the first-line nonsquamous NSCLC setting, across all PD-L1 subgroups. In the landmark analysis, you see an approximate doubling in the 12-month and a tripling in the 18-month progression-free survival rate," said lead author Mark A. Socinski, MD, Executive Medical Director of the Florida Hospital Cancer Institute, Orlando, Florida.

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For the primary endpoint analysis, patients with EGFR and ALK mutations were excluded. They comprised about 13% of the study participants. When patients with EGFR- or ALK-mutated NSCLC were included in the intent-to-treat analysis, the median overall survival was even higher with ABCP than BCP. 19.8 months vs 14.9 months. Patients with liver metastases also had improved median overall survival with the four-drug regimen over the three-drug regimen (13.2 months vs 9.1 months).

2018 ASCO-SITC Symposium

Trivalent CAR T-Cell Design May Enhance Antitumor Efficacy in Acute Lymphoblastic Leukemia

2018 ASCO SITC,Abstract 121., Fousek K

A novel approach to chimeric antigen receptor (CAR) T-cell therapy seems to effectively target acute lymphoblastic leukemia (ALL) cells with varying antigen profiles and may help to overcome antigen escape, seen with CD19-targeted therapy. According to data presented at the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium, by targeting CD19, CD20, and CD22 antigens with trivalent CAR T cells, researchers have managed to mitigate CD19-negative relapse in a laboratory study, resulting in enhanced antitumor efficacy.1 This strategy has the potential for use as an initial CAR T-cell therapy in relapsed ALL or a salvage therapy for patients with CD19-negative disease, the authors noted.

Testing for PD-L1 Amplification May Help Predict Response to Immune Checkpoint Blockade in Solid Tumors

2018 ASCO SITC,Abstract 47., Goodman AM

Analysis of more than 100,000 patients with cancer for gene CD274 (programmed cell death ligand 1 [PD-L1]) amplification may have implications for treatment with immune checkpoint blockade. Although shown to be rare in solid tumors, copy number alterations in PD-L1 genes were present in more than 100 unique solid tumor histologies. According to data presented at the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium, 67% of patients with solid tumors with PD-L1 amplification responded to programmed cell death protein 1 (PD-1)/PD-L1 blockade, with a median progression-free survival of 15.2 months.1 These responses appeared to be independent of tumor mutational burden, the authors noted.

Combination PARP and PD-1 Inhibition Shows Antitumor Activity in Advanced Malignancies

2018 ASCO SITC,Abstract 48., Friedlander M,

In a phase I trial of patients with advanced solid tumors, the combination of pamiparib (BGB-290), a selective poly (ADP-ribose) polymerase (PARP) inhibitor, and tislelizumab (BGB-A317), an agent targeting the programmed cell death protein 1 (PD-1) receptor, was well tolerated while demonstrating antitumor activity.1 According to data presented at the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium, 10 patients (23%) had a confirmed complete or partial response, and responses were observed in patients with wild-type and mutant BRCA status.

Combination Radiotherapy and Immunotherapy Appears Safe and Clinically Active in Advanced Solid Tumors

2018 ASCO SITC,Abstract 20., Lemons J

Results from the first and largest prospective trial to determine the safety of multisite ablative stereotactic body radiotherapy (SBRT) in combination with anti–programmed cell death protein 1 (anti–PD-1) immunotherapy pembrolizumab (Keytruda) suggest the combination regimen may improve outcomes in patients with advanced solid tumors and multiple metastatic sites.1 According to data presented at the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium, SBRT prior to pembrolizumab treatment was well tolerated, with no

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radiation dose reductions, and the overall objective response rate was 13.2% in the 68 patients with imaging follow-up. Moreover, when defined as a 30.0% reduction in any single nonirradiated measurable lesion, the abscopal response was present in 26.9% of patients, the authors noted.

Responses Reported With CAR T-Cell Therapy in High-Risk NHL

2018 ASCO SITC,Abstract 120., Abramson JS

LISOCABTAGENE MARALEUCEL (Liso-cel; JCAR017), a CD19-directed chimeric antigen receptor (CAR) T-cell therapy with defined composition, has shown "potent and durable" responses in poor-prognosis patients with relapsed or refractory aggressive non-Hodgkin lymphoma (NHL) in a phase I trial.1 According to data presented at the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium, toxicities were also manageable at all dose levels tested, with low rates of severe cytokine-release syndrome (1%) and neurotoxicity (12%).

2018 ASCO GI Symposium Highlight

Keytruda-Inlyta Combo Extends Survival in Advanced Renal Cell Carcinoma Patients, Phase 3 Trial Shows

ASCO GI Abstract 579., Atkins MB

A combination of Keytruda (pembrolizumab) and Inlyta (axitinib) significantly extended the lives of patients with advanced renal cell carcinoma (RCC) and delayed disease progression or death, according to a Phase 3 clinical trial.

The randomized trial, called KEYNOTE-426 (NCT02853331), examined the combination versus the standard of care Sutent (sunitinib) as a first-line treatment for advanced RCC patients. The combination also met its secondary objective of overall response rate, with more patients responding to it than to Sutent.

"Keytruda, in combination with the tyrosine kinase inhibitor Inlyta, resulted in significant and clinically meaningful improvements in overall survival, progression-free survival and objective response in this Phase 3 study.This marks the first time that combination treatment with an anti-PD-1 therapy has achieved the dual primary endpoints of overall survival and progression-free survival as first-line therapy in advanced renal cell carcinoma.

In a prior Phase 1b trial (NCT02133742), sponsored by Pfizer and Merck, researchers had already seen that a combination of Keytruda and Inlyta had promising anti-tumor activity, when given to untreated advanced RCC patients. In the open-label trial, 73% of patients experienced tumor reduction, including four complete responses and 34 partial responses. An additional eight patients achieved stable disease.

Based on those findings, Merck designed KEYNOTE-426 to determine if the combination outperformed the standard of care Sutent in these patients.

The study recruited 861 patients who were randomly assigned Keytruda, given into the vein every three weeks, in combination with oral Inlyta twice a day, or oral Sutent once a day. The study is now ongoing, with an estimated completion date in January 2020.

In addition to survival, progression-free survival, and overall response rates — all of which were met — the trial is also examining the duration of response, disease control rate, and safety as secondary measures.

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