Lung India

Official Publication of Indian Chest Society



Pub Med

www.lungindia.com



Editorial

Liquid biopsy for T790M mutation detection: A ray of hope?

1

3

19

24

Anant Mohan, Saurabh Mittal

Original Articles

A comparison of three strategies for withdrawal of noninvasive ventilation in chronic obstructive pulmonary disease with acute respiratory failure: Randomized trial

Kavitha Venkatnarayan, Gopi C Khilnani, Vijay Hadda, Karan Madan, Anant Mohan, Ravindra M Pandey, Randeep Guleria

Clinical profile and course of children with postinfectious bronchiolitis obliterans from a tertiary care hospital

Krishna Mohan Gulla, Kana Ram Jat, Rakesh Lodha, Sushii K Kabra

T790M mutations identified by circulating tumor DNA test in lung adenocarcinoma patients who progressed on first-line epidermal growth factor receptor-tyrosine kinase inhibitors

Vinodini Merinda, Gatot Soegiarto, Laksmi Wulandari

Predictors of mortality in acute exacerbations of chronic obstructive pulmonary disease using the dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation score

Avya Gopal Bansal, Gajanan S Gaude

Comparison of tuberculin skin test and QuantiFERON-TB Gold In-Tube test in Bacillus Calmette—Guerin-vaccinated children

Ira Shah, Jagdish Kathwale, Naman S Shetty

Regression equations of respiratory impedance of Indian adults measured by forced oscillation technique

Sajal De, Nalok Banerjee, Gagan Deep Singh Kushwah, Dharmendra Dharwey

> And More.... ISSN: 0970-2113

> > Medknow

- DLog in
- . 0
- Register (https://journals.lww.com/lungindia/pages/register.aspx? ContextUrl=%2flungindia%2fpages%2feditorialboard.aspx)
- Get new issue alertsGet alerts
- Submit a Manuscript (https://review.jow.medknow.com/lungindia)

Secondary Logo

(http://wolterskluwer.com/) Q

Journal Logo

(https://journals.lww.com/lungindia/pages/default.aspx)

Articles

Search

Q

Advanced Search (https://journals.lww.com/lungindia/pages/advancedsearch.aspx)

Editorial Board

Editor-In-Chief

Dr. Parvaiz Koul

Professor and Head

Pulmonary and Internal Medicine, Infectious Diseases/Geriatrics

SheriKashmir Institute of Medical Sciences,

Soura, Srinagar, J&K-190011,

INDIA

Deputy Editor

Dr. Bharat Bhushan Sharma

Associate Editors

Dr Prashant Chhajed

Dr Ritesh Agarwal

Dr Sundeep Salvi

Assistant Editor

Dr. Sheetu Singh

Dr. Karan Madan

Editorial Board Members

International

Dr. Sonia Buist, USA

Dr. Surya Bhatt, USA

Dr. Jerry A. Krishnan, USA

Dr. R. Dhand, USA

Dr. S. Kalra, USA

Dr. D. Honeybourne, UK

Dr. P. Nair, Canada

Dr. B. Jonson, Sweden

Dr. R. Pawankar, Japan

Dr. M. Azizur Rahman, Bangladesh

National

Dr. Virendra Singh

Dr. A. A. Mahashur

Dr. D. Ganguly

Dr. S. K. Jindal

Dr. S. K. Luhadia

Dr. R. Prasad

Dr. S. C. Matah

Dr. Rajesh Swarnakar

Dr. A. K. Janmeja

Dr. T. Mohan Kumar

Dr. V. Thanasekaraan

Dr. Surya Kant

Dr. Salil Bhargava

Dr. K. B. Gupta

Dr. Rajeev Gupta

Dr. R. Chowgule

Dr. J. C. Suri

Dr. N. K. Jain

Dr. J. M. Joshi

Dr. G N Srivastava

Section Editors

Alveolar diseases

Dr. C. Ravindran

Dr. M. Sabir

Critical care

Dr. G. C. Khilnani

Dr. Mradul K. Daga

Infectious diseases

Dr. A. G. Ghoshal

Dr. Ashok Shah

Lung cancer

Dr. D. Behera

Dr. Prasanta Mohapatra

Obstructive airway diseases

Dr. J. K. Samaria

Dr. Raja Dhar

Research methods

Dr. D.K. Mangal

Dr. Mohan Bairwa

Pictorial quiz

Dr. Alladi Mohan

Dr. R. Narasimhan

Pleural diseases

Dr. P. Baruwa

Dr. Arun Madan

Dr. Dharmesh Patel

Pulmonary circulation

Dr. P. Bhattacharyya

Dr. S. K. Chhabra

Sleep medicine

Dr. R. Guleria

Dr. Dhruv Chaudhary

Tuberculosis

Dr. S. K. Sharma

Dr. S. K. Katiyar

Surgical aspects of pulmonary medicine

Dr. S. K. Sarkar

Dr Apar Jindal

Interventional Pulmonology

Dr Nagarjun Maturu

Dr. Rakesh Chawla

Dr. Ramakant Dixit

Institutional affiliations: Editorial board members of Lung India

Editorial Board member

EDITOR-IN-CHIEF

Dr. Parvaiz Koul

DEPUTY EDITOR

Dr. Bharat Bhushan Sharma

ASSOCIATE EDITORS

Dr. Prashant Chhajed

Dr. Ritesh Agarwal

Dr. Sundeep Salvi

ASSISTANT EDITOR

Dr. Sheetu Singh

Affiliations

Professor & Head, Department of Internal & Pulmonary Medicine, Registrar, academics, Sher-i-Kashmir Institute

of Medical Sciences, Srinagar, India

Professor of Medicine, Head of Allergy & Pulmonary Division, Department of Medicine, SMS Medical College,

Jaipur, India

Fortis Hospitals, Mumbai and Navi Mumbai, Institute of Pulmonology, Medical Research and Development,

Mumbai, India

Professor, Dept of Pulmonary Medicine Postgraduate Institute of Medical Education and Research, Chandigarh,

India

CRF - Chest Research Foundation, Marigold Premises, Behind Gold AD Labs, Kalyani Nagar, Pune, India

Assistant professor, Department of Chest & Tuberculosis, Institute of Respiratory Diseases, SMS Medical College, Jaipur, India

EDITORIAL BOARD MEMBERS International

Dr. Sonia Buist

Dr. Surya Bhatt

Dr. R. Dhand

Dr. Jerry A. Krishnan

Dr. S. Kalra

Dr. D. Honeybourne

Dr. P. Nair

Dr. B. Jonson

Dr. R. Pawankar

Dr. M. Azizur Rahman

National

Dr. Virendra Singh

Dr. A. A. Mahashur

Dr. D. Ganguly

Dr. S. K. Jindal

Dr. S. K. Luhadia

Dr. R. Prasad

Dr. S. C. Matah

Dr. Rajesh Swarnakar

Professor Emeritus of Medicine, Pulmonary & Critical Care Medicine, Oregon Health & Science University, 3181 SW Sam Jackson Park Rd. MC:UHN67, Portland, OR, USA.

Assistant Professor, Medical Director, Pulmonary Function and Exercise Physiology Lab, Medical Director, Remote Pulmonary Rehabilitation Program Director, UAB Lung Imaging Core231 Kracke Building, Division of Pulmonary, Allergy and Critical Care Medicine, University of Alabama at Birmingham

Pulmonologist in Knoxville, Tennessee University of Tennessee Medical Center, USA.

University of Illinois Hospital, Chicago, National Institutes of Health (NIH), 1801 West Taylor Street, Chicago, IL, USA.

Rush-Copley Medical Center, Aurora, IL, USA. Consultant physician at Birmingham Heartlands Hospital, UK.

Professor of Medicine, Division of Respirology, Adjunct Professor of Medicine, McGill University, Staff Respirologist, Firestone Institute for Respiratory Health, Canada.

University Hospital, Lund, Sweden.

Prof. Ruby Pawankar, Prof. Allergy, Dept. of Pediatrics, Nippon Medical School, Tokyo, Japan.

Associate Professor, Respiratory Medicine, Under Faculty of Medicine, Dhaka University, Dhaka, Bangladesh.

Specialist in Respiratory Diseases and Director of Asthma Bhawan, Jaipur, Rajasthan, India Consultant Chest Physician, P.D. Hinduja National Hospital and MRC, II Floor, OPD Building, Veer Savarkar Marg, Mahim (W), Mumbai, India

 G D Hospitals & Diabetic Institute, Kolkata 2. Calcutta Heart Clinic & Hospital - Salt Lake Kolkata, India Emeritus Professor, Pulmonary Medicine Postgraduate Institute of Med Edu & Res, Chandigarh, India, Medical

Director, Jindal Clinics, Chandigarh, India.

Professor and Head, Department of Respiratory Medicine, Geetanjali Medical College and Hospital,

Udaipur, Rajasthan, India

King George's Medical University, (Erstwhile Chhatrapati Shahuji Maharaj Medical University), Chowk, Lucknow,

Uttar Pradesh, India

Professor of Chest Diseases, Department of TB & Chest Diseases, SSH, IMS BHU.

Director & Chief Consultant Pulmonologist, Department of Respiratory, Critical Care & Sleep Medicine with

Interventional Pulmonology, Getwell Hospital & Research Institute, Dhantoli, Nagpur - 440012, Maharashtra, India

10/03/22 10.11

Dr. A. K. Janmeja

Dr. T. Mohan Kumar

Dr. V. Thanasekaraan

Dr. Surya Kant

Dr. Salil Bhargava

Dr. K. B. Gupta

Dr. Rajeev Gupta

Dr. R. Chowgule

Dr. J. C. Suri

Dr. N. K. Jain

Dr. J. M. Joshi

Dr. G. N. Srivastava

SECTION EDITORS Alveolar diseases

Dr. C. Ravindran

Dr. M. Sabir

Critical care

Dr. G. C. Khilnani

Dr. Mridul Daga

Infectious diseases

Editorial Board : Lung India

Government Medical College & Hospital, Sector- 32,

Chandigarh Punjab-Haryana, India

Senior Consultant Pulmonologist & HOD, Sri

Ramakrishna Hospital Avarampalayam road, Coimbatore

641046, Tamilnadu, India

Emeritus Professor of Pulmonology, Sri Ramachandra

University, Head of Clinical Services, Respiratory

(Pulmonary) Medicine, Sri Ramachandra Medical Centre,

Porur, Chennai, India

King Georges Medical University, Lucknow, Chowk,

Lucknow, Uttar Pradesh, India

Professor & Head of Pulmonary Medicine, M.G.M.

Medical College, Indore, MP, India

Head, Dept. of Respiratory Medicine, Post Graduate

Institute of Medical sciences, Rohtak, Haryana, India

Chairman- Preventive Cardiology, General Medicine &

Research Eternal Hospital, 3 A Jagatpura Road, Near

Jawahar Circle, Jaipur, India

Head, Lung Care Clinic, Sukh Sagar Building, N S Patkar

Marg, Grant Road, Mumbai, Former Professor and Head

of Medicine Department, Bombay Hospital Institute of

Medical Sciences, Mumbai, India

Consultant, Professor & Head, Dept. of Pulmonary,

Critical Care & Sleep Medicine, Vardhman Mahavir

Medical College & Safdarjung Hospital, New Delhi, India

Director, Jain Chest Care Center, H, 28-32, Subhash

Nagar Shopping Center, Jaipur, India

Professor and Head, Department of Pulmonary Medicine,

TN Medical College, BYL Nair Hospital, Mumbai, India

Head and professor, Department of TB & Respiratory Disease, Institute of Medical Sciences, Banaras Hindu

University, Varanasi, India, and Deputy Medical

Superintendent (MM), SSL Hospital IMS, BHU, Varanasi

Uttar Pradesh, India

Professor & Head of Pulmonary Medicine and Vice Dean, DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India

Visiting Prof., Dept. of Medicine, MAMC, Agroha, Retd. Prof. and Head, Resp. Div., Dept. of Medicine, S.P. Medical College, Bikaner, Senior Consultant Physician & Pulmonologist, KMRI, Bikaner, Rajasthan, India

Professor & Head Department of Pulmonary Medicine & Sleep Disorders, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India

Director Professor of Medicine , And Incharge Medical ICU , Maulana Azad Medical College and attached Lok Nayak and GB Pant hospital , New Delhi, India

Dr. A. G. Ghoshal

Dr. Ashok Shah

Lung cancer

Dr. D. Behera

Dr. Prasanta Mohapatra

Obstructive airway diseases

Dr. J. K. Samaria

Dr. Raja Dhar

Research methods

Dr. D.K. Mangal

Dr. Mohan Bairwa

Pictorial quiz

Dr. Alladi Mohan

Dr. R Narashiman

Pleural diseases

Dr. P. Baruwa

Dr. Arun Madan

Dr. Dharmesh Patel

Pulmonary circulation

Dr. P. Bhattacharyya

Dr. S. K. Chhabra

Sleep medicine

Editorial Board : Lung India

Medical Director, National Allergy Asthma Bronchitis Institute, 11/3, Dr. Biresh Guha Street, 2nd Floor, IMA House, Park Circus, Kolkata, India Prof. Ashok Shah, Senior, Consultant, Department of Pulmonology, Max Super Specialty Hospital, Shalimar Bagh, Delhi, India

Senior Professor & Head, Dept. of Pulmonary Medicine, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Professor and Head, Dept. of Pulmonary Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

Ex-Professor & Head, Department of Chest Diseases, Institute of Medical Sciences, B.H.U., Varanasi, India Director, Department of Pulmonology, C K Birla group of Hospitals, Kolkata, India

Professor and Dean Research, IIHMR University, Jaipur, 1, Prabhu Dayal Marg, Near Sanganer Air Port, Jaipur-302029, Rajasthan, India

Affiliation 1: Assistant Professor of Epidemiology, Department of Public Health, IIHMR University, Jaipur, India, Affiliation 2: Associate, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA.

Professor and Head, Department of Medicine; Chief, Division of Pulmonary, Critical Care and Sleep Medicine, Sri Venkateswara Institute of Medical, Sciences, Tirupati 517 507 Andhra Pradesh, India Senior Respiratory Physician, Apollo Hospitals, Chennai, India

Module no. 1, 1st floor, Astha Towers, C K Road, Panbazar, Near Hari Sabha Guwahati, Assam, India Professor & HOD, Dept. of Pulmonary Medicine, NDMC Medical College, HRH, Civil Lines, New Delhi, India Consultant Respiratory Physician, City Clinic & Bhailal Amin General Hospital, Vadodara, Gujarat, India

Consultant, Institute of Pulmocare and Research, Kolkata. Add: DG8, Action area 1, New Town, Kolkata, India

Head, Dept. of Pulmonary, Sleep & Critical Care Medicine, Primus Super Specialty Hospital, Chanakyapuri, New Delhi, Former Director-Prof. Vallabhbhai Patel Chest Institute, Delhi, India Editorial Board : Lung India

Dr. R. Guleria

Professor, Department of Pulmonary Medicine & Sleep Disorders, All India Institute of Medical Sciences(AIIMS), New Delhi, India

Director, All India Institute of Medical Sciences (AIIMS),

Dr. Dhruv Chaudhary

Sr. Prof. & Head PCCM, Pt. B.D.S. Post Graduate Institute of Medical Sciences (PGIMS) Rohtak, Haryana, India

Tuberculosis

Adjunct Professor, Dept. of Molecular Medicine, Jamia Hamdard Institute of Molecular Medicine, Hamdard University, Hamdard Nagar, Delhi & Director Research. & Adjunct Professor, Departments of General Medicine & Pulmonary Medicine, JNMC, Datta Meghe Institute of Medical Sciences (DMIMS), Sawangi (M),

Dr. S. K. Sharma

Wardha (Maharashtra), India Former Principal & Dean, Professor & Head, Dept. of Tuberculosis & Respiratory Diseases. GSVM Medical College, Kanpur, India

Dr. S. K. Katiyar

C-24, Vaishali Marg, Vaishali Nagar, Jaipur, Rajasthan 302021, India

Surgical aspects of pulmonary medicine

Director - Advanced Lung Failure, Transplant Pulmonology, Yashoda Hospital, Hyderabad, India

Dr. S. K. Sarkar

Director and Head, Department of Interventional

Dr. Apar Jindal

Pulnonology, Yashoda Hospitals, Somajiguda, Hyderabad, India

Interventional pulmonology

Sr. Consultant Respiratory Medicine, Critical Care and Sleep Medicine, Interventional Pulmonologist, Jaipur Golden Hospital, Saroj Hospital & Rajiv Gandhi Cancer Institute, Delhi, India

Dr. Nagarjun Maturu

Professor & Unit Head, Department of Respiratory Medicine, J. L. N. Medical College & Associated Group of Hospitals, Ajmer, Rajasthan, India

Dr. Rakesh Chawla

Dr. Ramakant Dixit



Never Miss an Issue

Get new journal Tables of Contents sent right to your email inbox Type your email

Get New Issue Alerts

Browse Journal Content

- Degin
- OT
- Register (https://journals.lww.com/lungindia/pages/register.aspx?
 ContextUrl=%2flungindia%2ftoc%2f2020%2f37010)
- Get new issue alertsGet alerts
- Submit a Manuscript (https://review.jow.medknow.com/lungindia)

Secondary Logo

(http://wolterskluwer.com/) Q

Journal Logo

(https://journals.lww.com/lungindia/pages/default.aspx) Articles

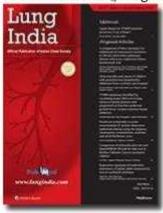
Search

Q

Advanced Search (https://journals.lww.com/lungindia/pages/advancedsearch.aspx)

Home (/lungindia/pages/default.aspx) > Jan-Feb 2020 - Volume 37 - Issue 1

< Previous Issue (/lungindia/toc/2019/36060) | Next Issue (/lungindia/toc/2020/37020) >



Jan-Feb 2020 - Volume 37 - Issue 1

pp: 1-96

₹≣ View Contributor Index (https://journals.lww.com/lungindia/pages/contributorindex.aspx?
year=2020&issue=37010)

□ Editorial

Liquid biopsy for T790M mutation detection: A ray of hope? (https://journals.lww.com/lungindia/Fulltext/2020/37010/Liquid_biopsy_for_T790M_r

Mohan, Anant; Mittal, Saurabh Lung India. 37(1):1-2, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00001)
- © Get Content & Permissions

 Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Liquid_biopsy_for_T790M_mutation_detection

Table of Contents Outline | Back to Top

☐ Original Article

A comparison of three strategies for withdrawal of noninvasive ventilation in chronic obstructive pulmonary disease with acute respiratory failure: Randomized trial (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_comparison_of_three_stra

Venkatnarayan, Kavitha; Khilnani, Gopi C; Hadda, Vijay; More Lung India. 37(1):3-7, Jan-Feb 2020.

- • BAbstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00002)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_comparison_of_three_strategies_for_withdra

Clinical profile and course of children with postinfectious bronchiolitis obliterans from a tertiary care hospital

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Clinical_profile_and_course_

Gulla, Krishna Mohan; Jat, Kana Ram; Lodha, Rakesh; More Lung India. 37(1):8-12, Jan-Feb 2020.

- • Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00003)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Clinical_profile_and_course_of_children_with.;

T790M mutations identified by circulating tumor DNA test in lung adenocarcinoma patients who progressed on first-line epidermal growth factor receptor-tyrosine kinase inhibitors

(https://journals.lww.com/lungindia/Fulltext/2020/37010/T790M_mutations_identified

Merinda, Vinodini; Soegiarto, Gatot; Wulandari, Laksmi Lung India. 37(1):13-18, Jan-Feb 2020.

- • Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00004)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/T790M_mutations_identified_by_circulating_tr

Predictors of mortality in acute exacerbations of chronic obstructive pulmonary disease using the dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation score (https://journals.lww.com/lungindia/Fulltext/2020/37010/Predictors_of_mortality_in_a

Bansal, Avya Gopal; Gaude, Gajanan S Lung India. 37(1):19-23, Jan-Feb 2020.

- • Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00005)
- · © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Predictors_of_mortality_in_acute_exacerbation

Comparison of tuberculin skin test and QuantiFERON-TB Gold In-Tube test in Bacillus Calmette—Guerin-vaccinated children

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Comparison_of_tuberculin_s

Shah, Ira; Kathwate, Jagdish; Shetty, Naman S Lung India. 37(1):24-29, Jan-Feb 2020.

- ⊕Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00006)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Comparison of tuberculin skin test and.6.asp

Regression equations of respiratory impedance of Indian adults measured by forced oscillation technique

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Regression_equations_of_res

De, Sajal; Banerjee, Nalok; Kushwah, Gagan Deep Singh; More Lung India. 37(1):30-36, Jan-Feb 2020.

- ⊞Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00007)
- © Get Content & Permissions
- Open

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Regression_equations_of_respiratory_impedance

Endoscopic ultrasound-guided-fine-needle aspiration/fine-needle biopsy in diagnosis of mediastinal lymphadenopathy – A boon

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Endoscopic_ultrasound_guid

Junare, Parmeshwar Ramesh; Jain, Samit; Rathi, Pravin; More Lung India. 37(1):37-44, Jan-Feb 2020.

- • Abstract
- ☆Favorites

- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00008)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Endoscopic_ultrasound_guided_fine_needle.8.a

Table of Contents Outline | Back to Top

Prevalence of pulmonary tuberculosis in India: A systematic review and meta-analysis (https://journals.lww.com/lungindia/Fulltext/2020/37010/Prevalence_of_pulmonary_ti

Sathiyamoorthy, Ramadass; Kalaivani, Mani; Aggarwal, Praveen; More Lung India. 37(1):45-52, Jan-Feb 2020.

- —Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00009)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Prevalence_of_pulmonary_tuberculosis_in_Ind

Table of Contents Outline | Back to Top

□ Case Report

Case of urinothorax – A rare presentation (https://journals.lww.com/lungindia/Fulltext/2020/37010/Case_of_urinothorax___A_r

Chawla, Aditya Kumar; Chaudhary, Gaurav; Chawla, Madhav Kumar; More Lung India. 37(1):53-56, Jan-Feb 2020.

- —Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00010)
- © Get Content & Permissions
- Open
 (https://journals.lww.com/lungindia/Fulltext/2020/37010/Case_of_urinothorax___A_rare_presentation.14

A case report evaluating combined effect of intensity-modulated radiotherapy and deep inspiratory breath-hold for mediastinal lymphoma: A dosimetric analysis (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_case_report_evaluating_ca

Dewan, Abhinav; Chufal, Kundan Singh; Tandon, Sarthak; More Lung India. 37(1):57-62, Jan-Feb 2020.

 • Abstract

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00011)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_case_report_evaluating_combined_effect_of.

A novel procedure of endobronchial ultrasound-guided transbronchial needle aspiration for pulmonary parenchymal lesions: The ZUTAM technique (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_novel_procedure_of_endo

Tamburrini, Mario; Reddy, Siva Prasad; Gundappa, Vivek; More Lung India. 37(1):63-65, Jan-Feb 2020.

- ⊞Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00012)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_novel_procedure_of_endobronchial.12.aspx)

Table of Contents Outline | Back to Top

⊟ Pictorial Quiz

Mediastinal mass mimic

 $(https://journals.lww.com/lungindia/Fulltext/2020/37010/Mediastinal_mass_mimic.13.$

Datta, Ananda; Patro, Mahismita; Gothi, Dipti Lung India. 37(1):66-68, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00013)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Mediastinal_mass_mimic.13.aspx)

Table of Contents Outline | Back to Top

□ Case Letters

A rare case of lung adenocarcinoma: Unusual presentation with miliary mottling (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_rare_case_of_lung_adeno

Goyal, Pankaj; Bothra, Sneha J; Jain, Parveen; More Lung India. 37(1):69-71, Jan-Feb 2020.

☆Favorites

- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00014)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/A_rare_case_of_lung_adenocarcinoma__Unust

Gefitinib-induced pyogenic granuloma in a patient with lung cancer (https://journals.lww.com/lungindia/Fulltext/2020/37010/Gefitinib_induced_pyogenic_

Sahoo, Satyajeet; Sirka, Chandra Sekhar; Majumdar, Saroj K Das; More Lung India. 37(1):71-72, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00015)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Gefitinib_induced_pyogenic_granuloma_in_a_l

From symptom and sign to diagnosis in a case of pulmonary plasmacytoma and pulmonary metastasis

(https://journals.lww.com/lungindia/Fulltext/2020/37010/From_symptom_and_sign_te

Ghinea, Mihaela Maria; Stoica, Andreea Georgiana; Ciocodei, Sabina Livia Lung India. 37(1):72-74, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00016)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/From_symptom_and_sign_to_diagnosis_in_a_

Table of Contents Outline | Back to Top

Research Letters

Osteosarcoma mimicking fibrous pleurisy with dystrophic calcification!!! (https://journals.lww.com/lungindia/Fulltext/2020/37010/Osteosarcoma_mimicking_fil

Kumar, Tahira Sultana; Chawla, Ashish Lung India. 37(1):75-76, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00017)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Osteosarcoma_mimicking_fibrous_pleurisy_wit

Osimertinib as an emerging therapeutic modality in nonsmall cell lung cancer: Opportunities and challenges in Indian scenario (https://journals.lww.com/lungindia/Fulltext/2020/37010/Osimertinib_as_an_emerging

Thakur, Sayanta; Chakraborty, Dwaipayan Sarathi; Lahiry, Sandeep; More Lung India. 37(1):77-78, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00018)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Osimertinib_as_an_emerging_therapeutic_mod

Intercostal chest drain clamping

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Intercostal_chest_drain_clan

Flores-Franco, René Agustin

Lung India. 37(1):79-80, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00019)
- · © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Intercostal_chest_drain_clamping.19.aspx)

The effects of obesity on pulmonary function in adults with asthma (https://journals.lww.com/lungindia/Fulltext/2020/37010/The_effects_of_obesity_on_1

Al-Mendalawi, Mahmood Dhahir

Lung India. 37(1):80-81, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00020)
- · © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/The_effects_of_obesity_on_pulmonary_function

Table of Contents Outline | Back to Top

(../../_controltemplates/OAKS.Journals/#)

- 1
- 2
- .

Show 20 results per page ➤ Show:

20 results per page

^Back to Top

- Degin
- OI
- Register (https://journals.lww.com/lungindia/pages/register.aspx?
 ContextUrl=%2flungindia%2ftoc%2f2020%2f37010)
- Get new issue alertsGet alerts
- Submit a Manuscript (https://review.jow.medknow.com/lungindia)

Secondary Logo

(http://wolterskluwer.com/) Q

Journal Logo

(https://journals.lww.com/lungindia/pages/default.aspx) Articles

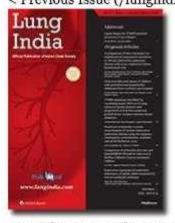
Search

Q

Advanced Search (https://journals.lww.com/lungindia/pages/advancedsearch.aspx)

Home (/lungindia/pages/default.aspx) > Jan-Feb 2020 - Volume 37 - Issue 1

< Previous Issue (/lungindia/toc/2019/36060) | Next Issue (/lungindia/toc/2020/37020) >



Jan-Feb 2020 - Volume 37 - Issue 1

pp: 1-96

Table of Contents Outline

Subscribe to eTOC

View Contributor Index (https://journals.lww.com/lungindia/pages/contributorindex.aspx? year=2020&issue=37010)

□ Correspondence

Assessing the flat diaphragm in chronic obstructive pulmonary disease: Deep-diving is a better approach

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Assessing_the_flat_diaphrag

Devaraj, Uma; Venkatnarayan, Kavitha; Krishnaswamy, Uma Maheswari; More Lung India. 37(1):82-83, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00021)

- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Assessing_the_flat_diaphragm_in_chronic.21.as

Ultrasonography of diaphragm in chronic obstructive pulmonary disease: Unanswered questions

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Ultrasonography_of_diaphra

Hadda, Vijay; Tiwari, Pawan; Mittal, Saurabh; More Lung India. 37(1):83-84, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00022)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Ultrasonography_of_diaphragm_in_chronic.22.

Ultrasonography in Chronic Obstructive Pulmonary Disease: Fact or Fiction? (https://journals.lww.com/lungindia/Fulltext/2020/37010/Ultrasonography_in_Chronic

Alqahtani, Jaber S; Alghamdi, Saeed M Lung India. 37(1):84-85, Jan-Feb 2020.

- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00023)
- © Get Content & Permissions
- Open (https://journals.lww.com/lungindia/Fulltext/2020/37010/Ultrasonography_in_Chronic_Obstructive_Pulm

Table of Contents Outline | Back to Top

□ General Perspective

Bronchial Thermoplasty for Severe Asthma: A Position Statement of the Indian Chest Society

(https://journals.lww.com/lungindia/Fulltext/2020/37010/Bronchial_Thermoplasty_for

Madan, Karan; Mittal, Saurabh; Suri, Tejas M; More Lung India. 37(1):86-96, Jan-Feb 2020.

- • Abstract
- ☆Favorites
- PDF (https://journals.lww.com/lungindia/_layouts/15/oaks.journals/downloadpdf.aspx?an=01408641-202037010-00024)
- © Get Content & Permissions

Table of Contents Outline | Back to Top (../../_controltemplates/OAKS.Journals/#)

T790M mutations identified by circulating tumor DNA test in lung adenocarcinoma patients who progressed on first-line epidermal growth factor receptor-tyrosine kinase inhibitors

Vinodini Merinda¹, Gatot Soegiarto², Laksmi Wulandari³

¹Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, ²Division of Clinical Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, ³Division of Thoracic Oncology, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

ABSTRACT

Background: Plasma circulating tumor deoxyribonucleic acid (ctDNA) test is an alternative method to detect the T790M mutation. Compared to conventional tumor rebiopsy, ctDNA possesses several advantages including less invasive, faster, lower costs, and having minimal risk of complications for patients. Objective: The main objective of the study is to identify the prevalence of T790M mutations in lung adenocarcinoma patients who progressed after tyrosine kinase inhibitors (TKIs) therapy using ctDNA examination. Materials and Methods: This was a retrospective cohort study based on medical records of lung adenocarcinoma patients in the Oncology Outpatient Clinic of Dr. Soetomo General Hospital within the period of January 2017—June 2018. Patients who progressed after receiving first-line epidermal growth factor receptor-TKI (EGFR-TKI) undergone plasma ctDNA examination and genotyping using digital platforms (Droplet Digital™PCR) method. Results: In total, there were 39 patients who met the criteria for ctDNA testing. Thirty-three patients (84.6%) received first-line gefitinib, while the other six (15.4%) received erlotinib. The T790M mutations were detected in 46.2% of patients. In addition, EGFR common mutation in exon 19 and exon 21 were detected in 87.2% of patients. Median progression-free survival of patients receiving first-line gefitinib or erlotinib were both around 9 months and did not differ significantly. Conclusions: CtDNA examination successfully detected T790M mutation in a certain proportion of lung adenocarcinoma patients who progressed after first-line EGFR-TKI without the need for difficult and invasive rebiopsy.

KEY WORDS: T790M mutation, first-line epidermal growth factor receptor-tyrosine kinase inhibitors, lung adenocarcinoma.plasma.circulating tumor deoxyribonucleic acid

Address for correspondence: Mrs. Laksmi Wulandari MD., PhD., FCCP, Division of Thoracic Oncology, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Academic Hospital, Jl. Mayjen Prof. Dr. Moestopo No. 6-8, Surabaya 60 28 5, Indonesia. E-mail: laksmi.wulandari.@fk.unair.ac.id

Received: 23-04-2019 Revised: 08-09-2019 Accepted: 12-10-2019 Published: 31-12-2019

INTRODUCTION

Lung cancer is one of the most common causes of cancer mortality in the United States. In 2018, the incidence of new lung cancer cases was estimated to be 234,030 (121,680



of men and 112,350 of women), and the mortality of lung cancer was estimated at 154,050 (83,550 of men and

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Merinda V, Soegiarto G, Wulandari L. T790M mutations identified by circulating tumor DNA test in lung adenocarcinoma patients who progressed on first-line epidermal growth factor receptor-tyrosine kinase inhibitors. Lung India 2020;37:13-8.

70,500 of women),^[1] Nonsmall-cell lung cancer (NSCLC) is considered as the most common type, which comprised more than 85% of all lung cancer cases,^[2] Adenocarcinoma is the most common type of lung cancer and is associated with the presence of epidermal growth factor receptor (EGFR) mutation in about 14%–19% of patients in the Western countries and in 40%–48% of patients in Asia,^[3]

The EGFR-tyrosine kinase inhibitors (EGFR-TKI), including gefitinib, erlotinib, and afatinib, are recommended as the first-line treatment for patients with positive EGFR-mutation. Despite achieving notable efficacy from EGFR-TKI treatment, a majority of patients eventually develop resistance after a median progression-free survival (PFS) of approximately 1-year (8-14 months). The progressive disease could be accounted to different resistance mechanisms to TKI. The most common resistance mechanism (approximately 60%) is the T790M secondary mutation. Consequently, patients who progressed after receiving first-line TKI therapy were subjected to rebiopsies of tumor tissue to determine the presence of T790M mutation. However, rebiopsy is not always feasible for many of the patients. [4]

One alternative method that could be employed for the detection of T790M is the circulating tumor deoxyribonucleic acid (ctDNA) test. The ctDNA genotyping is a specific and sensitive biomarker test that can be used for the detection of EGFR mutation. The ctDNA can be extracted from plasma and used for tumor-specific molecular marker detection. Compared to conventional rebiopsy of tumor tissue in patients who have progressed, ctDNA possesses several advantages such as less invasive, faster, lower costs, and having minimal risk of complications for patients. The concordance between plasma ctDNA test and tumor rebiopsy result in NSCLC patients in Asia Pacific was found to be 78%, with a sensitivity of 50% and specificity of 97%.[3] T790M was detected in 47% of NSCLC patients with acquired EGFR-TKI resistance using the plasma ctDNA test and can be found either before or after disease progression. Hence, it can be regarded as a poor prognostic factor.[5]

Until now, the T790M mutation in NSCLC patients in Dr. Soetomo General Hospital, Surabaya, Indonesia, had never been reported. The aim of this study is to determine the prevalence of T790M and other EGFR mutations in lung adenocarcinoma patients who progressed after the first-line EGFR-TKI using ctDNA test.

MATERIALS AND METHODS

This was a retrospective cohort study based on the medical records of lung adenocarcinoma patients in the Oncology Outpatient Clinic of Dr. Soetomo General Hospital, Surabaya, Indonesia, a tertiary referral hospital in Indonesia, within the period of January 2017 to June 2018. Eligible participants must fulfill the inclusion

criteria: those who had been diagnosed with pulmonary adenocarcinoma Stage IV, had positive EGFR mutation, treated and followed-up at the Oncology Outpatient Clinic of Dr. Soetomo General Hospital Surabaya, Indonesia, received first-line EGFR-TKI as treatment, had their disease progressed as evident by radiological (RECIST version 1.1) and/or physician's clinical judgment, and subsequently undergone plasma ctDNA examination. All of the participants characteristic and demographic data, EGFR mutation status, types of first-line EGFR-TKI received, and survival data were recorded. All of the data were obtained from the patient's medical record, Participants with incomplete data or had their plasma ctDNA examination done while on chemotherapy were excluded from the study. This study was approved by the Ethical Committee of Dr. Soetomo General Hospital, Surabaya, Indonesia (0632/KEPK/Ix/2018).

During the study period, from the first screening, there were a total of 50 patients who had their plasma ctDNA tested and were recorded in the medical records. Eleven patients were excluded due to several reasons, leaving 39 patients who met the inclusion criteria and included in the study as described in Figure 1. We describe our study and the participants filled out the consent form.

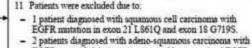
Briefly, the procedure for ctDNA test in our hospital was as follows: blood samples were taken from all of the patients and put in ethylenediaminetetraacetic acid tubes. The samples

- · Non-small cell hung cancer patients with positive EGFR mutation,
- · Received EGFR-TKI treatment
- Comply to follow-up visit and monitoring at Oncology Outpatient
- Clinic of Dr. Soetomo General Hospital, Surabaya

 Subsequently had disease progression (evident by RECIST version 1.1)
- and/or by physician's clinical judgement)

 Had plasma ctDNA test at Dr. Soetomo General Hospital, Surabaya from January 2017 to June 2018

50 patients



- EGFR exon 19 deletion mutation and have received EGFR-TKI as first line treatment.

 1 patient diagnosed with squamous cell carcinoma and
- 1 patient diagnosed with squamous cell carcinoma and received chemotherapy for 6 cycles. Repeated biopsy was conducted with a diagnosis of squamous cell carcinoma with EGFR mutation in exon 19. Patient received EGFR-TKI as the second line treatment.
- 1 patient diagnosed with squamous cell carcinoms and received 6 cycles of chemotherapy. Repeated biopsy was conducted with a diagnosis of adenocarcinoms with EGFR mutation in exon 19. Patient received EGFR-TKI as the second line treatment.
- 6 patients who had their ctDNA test during the period of the second-line chemotherapy treatment

Total of 39 patients who fulfilled the inclusion criteria

Figure 1: Flowchart of patient recruitment

were then directly sent to a central referral laboratory for further processing within 2 h of blood drawing. Plasma was obtained after a series of centrifugations according to the standard protocol. Fresh plasma were stored at −80°C until further examination. DNA extractions were carried out by using spin column method with QIAamp[®] circulating nucleic acid kit (QIAGEN, Manchester, UK). Extracted ctDNAs were tested for EGFR mutations using digital detection with the highly sensitive and quantitative Droplet Digital PCR (ddPCR[™]; Bio-Rad/Molecular MD, Hercules, CA, USA). Assays were performed according to the manufacturer's protocol.

The collected data were assessed using the Shapiro-Wilk test for normality of the distribution. We use the Mann–Whitney U-test or Independent t-test to assess the difference between patients who received first-line gefitinib or erlotinib in terms of PFS, with P < 0.05 considered as statistically significant. All of the statistical analysis was done using IBM SPSS Statistics Software Version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Subjects characteristics

The characteristics of the study participants were summarized in Table 1. The average age of the participant was 57.80 ± 11.29 years (ranged from 35 to 83 years). The majority of them (20 individuals, 51.3%) were in 41-60 years age group. Most of them were female (28 individuals, 71.8%) and nonsmokers (29 individuals, 74.4%). Based on the data of the initial performance score (PS), the majority of the study participants had PS 1 condition (34 individuals, 87.2%).

Most of the histopathology specimens were taken from lung mass (30 samples, 76.9%), mostly by fine-needle aspiration biopsy (FNAB) techniques (in 23 participants, 59.0%). The first-line EGFR-TKI treatment received by the participants was mostly gefitinib (in 33 patients, 84.6%). With respect to EGFR mutation type, EGFR common mutations were a dominant finding (87.2%), consisted of 23 patients with exon 19 deletion mutation (59.0%) and 11 patients with exon 21 L858R mutation (28.2%).

T790M mutation status

The result of the T790M mutation status obtained from plasma ctDNA test in this study was illustrated in Table 2. Eighteen out of 39 patients (46.2%) showed positive T790M mutation. Comparing participants with T790M-positive and T790M-negative mutations, there were no significant differences in patient's characteristics in terms of age group, sex, smoking history, and first-line EGFR-TKI treatment received [Table 3].

Progression free survival

In this study, 3 out of 39 participants who fulfill the inclusion criteria had incomplete survival data, so they

Table 1: Baseline characteristics of the study participants

Characteristics	и (%)
Age category (years)	
21-40	3 (7.7)
41-60	20 (51.3)
61-80	15 (38.5)
>80	1(2.6)
Sex	0.50000000
Women	28 (71.8)
Men	11 (28.2)
Smoking history	33.5000
Nonsmoker	29 (74.4)
Ex-smoker	4 (10.3)
Smoker	6 (15.4)
Performance status (WHO)	20000000000
1	34 (87.2)
2	4 (10.3)
3	1 (2.9)
Histopathological sampling site	
Lung mass	30 (76.9)
Organ metastasis	7 (17.9)
Lung mass and organ metastasis	2 (5.1)
Histopathological sampling method	110000000000000000000000000000000000000
Fine-needle aspiration	23 (59.0)
Bronchoscopy	4 (10.3)
Pleural effusion	3 (7.7)
Fine-needle aspiration and bronchoscopy	5 (12.8)
Fine-needle aspiration and pleural effusion	2 (5.1)
Other (open biopsy)	2 (5.1)
EGFR mutation status	
Exon 18 G719S	2 (5.1)
Exon 19 deletion	23 (59.0)
Exon 21 L858R	11 (28.2)
Exon 19 deletion and exon 21 L858R	I (2.6)
Exon 20 and exon 21 L858R	1 (2.6)
Exon 20, exon 19 deletion and exon 21 L861Q	1(2.6)
First-line EGFR-TKI treatment	
Gefitinib	33 (84.6)
Erlotinib	6 (15.4)

EGFR: Epidermal growth factor receptor, TKI: Tyrosine kinase inhibitors

Table 2: Result of circulating tumor DNA plasma test

Plasma ctDNA test and its mutation profiles	н (%)
Results of plasma ctDNA test	
T790M mutation (+)	18 (46.2%)
T790M mutation (-)	21 (53.8%)
Mutation profile of plasma ctDNA test	
T790M mutation (-)	15 (38.5%)
T790M mutation (-) and exon 19 deletion	5 (12.8%)
T790M mutation (-) and exon 21 L585R	1 (2.6%)
T790M mutation (+)	7 (17.9%)
T790M mutation (+) and exon 19 deletion	7 (17.9%)
T790M mutation (+) and exon 21 L858R	4 (10.3%)

ctDNA: Circulating tumor DNA

were not included in the analysis of the PFS. With regard to patients who had disease progression, the median PFS was 9 months and the 12 months survival rate was 36.1% [Table 4]. There was no difference in the median PFS between the two types of EGFR-TKI treatment (gefitinib or erlotinib). The median PFS value for both types of EGFR-TKI treatment was around 9 months (P = 0.932) as shown in Table 5.

DISCUSSION

Plasma ctDNA test in lung adenocarcinoma patients who had progressive disease following the first-line EGFR-TKI in Dr. Soetomo General Hospital Surabaya, Indonesia, revealed 46.2% prevalence of positive T790M mutation, This result is encouraging because our study confirmed the conclusions of many other previous studies done in similar circumstances elsewhere.[6-9] It has long been known that EGFR-mutant lung cancer patients who received EGFR-TKI treatment will eventually come to a disease progression due to secondary resistance to EGFR-TKI.[10] Current guidelines recommended tumor tissue rebiopsy to analyze the mechanisms of resistance and identify new targets for further therapy.[11-13] However, it is not easy to obtain tumor samples from patients with EGFR mutation-positive NSCLC that has relapsed after treatment with EGFR-TKIs. The confirmation that plasma ctDNA analysis using digital assay can be used as an alternative and noninvasive method to assess EGFR secondary mutation is a major advance in the management of NSCLC patients. It diverts the necessity of other cumbersome and invasive method which is also vulnerable to false-negative results.

Table 3: Characteristics of T790M-positive and T790M-negative mutant patients

Characteristics	T790M (-)	T790M (+)	P
Age category (years), n (%)			
21-40	0	3 (16.7)	0.237
41-60	12 (57.1)	8 (44.4)	
61-80	8 (38.1)	7 (38.9)	
≥80	1 (4.8)	0	
Sex, n (%)			
Woman	15 (71.4)	13 (72.2)	1.0
Man	6 (28.6)	5 (27.8)	
Smoking history, n (%)		entresent.	
Nonsmoker	16 (76.2)	13 (72.2)	0.792
Ex-smoker	2 (9.5)	2 (11.1)	
Smoker	3 (14.3)	3 (16.7)	
First-line EGFR-TKI treatment, n (%)	55500000	1000000	
Gefitinib	18 (85.7)	15 (83.3)	1.0
Erlotinib	3 (14.3)	3 (16.7)	

EGFR: Epidermal growth factor receptor, TKI: Tyrosine kinase inhibitors

Table 4: Progression-free survival analysis

Analysis of patient's survival	Value
PFS-months	000
Median	9
Range	2-48
PFS in 12 months, n (%)	
<12	23 (63.9)
>12	13 (36.1)

PFS: Progression-free survival

Table 5: Median progression-free survival of first-line gefitinib or erlotinib treatment

First-line EGFR-TKI treatment	Median PFS months (range)	P
Gefitinib	9 (2-48)	0.932
Erlotinib	9 (3-16)	

PFS: Progression-free survival, TKI: Tyrosine kinase inhibitors, EGFR: Epidermal growth factor receptor Plasma ctDNA analysis is now approved as a robust and accurate method for the detection of actionable mutations prior treatment, selection of first-line TKI, predicting and monitoring response to treatment, and emerging drug resistance mechanisms in NSCLC.[12,14] Many studies had confirmed the high sensitivity and specificity of plasma ctDNA analysis, [8,5] which also showed high overall concordance with tumor tissue samples.[8,15] NSCLC patients from our hospital had previously been involved in a large multicenter IGNITE study conducted in 90 centers from Asia-Pacific and Russia.[3] In that study, plasma ctDNA also had a high concordance with matched tissue/ cytology samples (80.5%) albeit with somewhat lower sensitivity (sensitivity 46.9%, specificity 95.6%). EGFR mutation frequencies for evaluable tissue/cytology samples in Asia-Pacific in that study were 49.3% (862/1749).[3]

The prevalence of EGFR mutation in our study is dominated by EGFR common mutation (87.2%) which consisted of exon 19 (59.0%) and exon 21 L858R mutation (28.2%). This result is consistent with other major researches in the field[16-20] which found that the prevalence of EGFR common mutation was around 85%-90%, consisting of exon 19 deletion and exon 21 L858R mutation. Similarly, in the IGNITE study, the proportion of EGFR common mutation was 91.2% in the Asia-Pacific population, which consisted of exon 19 deletion (48.7%) and exon 21 L858R mutation (42.5%).[3] In our study, exon 18 G719S mutation comprised 5.1% of the mutation pool, whereas combination of exon 19 deletion and exon 21 L858R mutation, exon 20 and exon 21 L858R mutation, and triple mutation of exon 19 deletion, exon 20 and exon 21 L861Q mutation were each 2.6% of our study participants, respectively. The result of our study is also consistent with the common findings as summarized by Sharma et al.[21] and Pirker et al., [22] where exon 18 mutation was found to be 5% for the total mutation pool and mutation in exon 20 were <1% in proportion. In the IPASS study, several patients were found to possess either EGFR mutation in exon 20, other types of mutations, and/or multiple combinations of mutations.[16] The mutation in exon 20 is associated with primary resistance to EGFR-TKL[23,24]

The presence of EGFR mutation in NSCLC of adenocarcinoma histology warrants EGFR-TKI as the first-line treatment.[11] With regard to the patient's demographic data, our study results were closely resembled or comparable to the IPASS and WJTOG3405 studies.[16,25] The subject's median age in our study was 58 years (ranged from 35 to 83 years), while in the IPASS study, the median age of the participants was 57 years (range: 24-84 years) and in WJTOG3405 study, it was 64 years (range: 34-74 years). A higher proportion of female patient (71.8%) was found in our study. This result was also similar with NEJ002 and WJTOG3405 studies. In NEJ002 study, the female participants made up 63.2% of the study population, [28] while in WJTOG3405 study, it was 68%.[25] In terms of smoking history, there were more nonsmokers (74.4%) compared to active and ex-smokers. The result of our study is similar to the WITOG3405

study where nonsmokers were found to be 70.9%. [25]
Most participants in our study were in PS 1 condition, which made up 87.2% of the total study population. In comparison, only 64.2% of study participants in IPASS study had PS 1 condition. [16] With regard to the sampling site of histopathological examination for the diagnosis of adenocarcinoma, most specimen samples in our study were obtained from lung mass (76.9%). The most common sampling method for histopathological examination was by FNAB (59%). This finding is consistent with the IGNITE study, where fine-needle aspiration was also identified as the most common method for obtaining samples (51%). [21]

Three types of EGFR-TKI available in Indonesia for first-line treatment of EGFR-mutant NSCLC were gefitinib, erlotinib, and afatinib. Gefitinib was more widely used (84.6%) than erlotinib. This could be due to the fact that gefitinib was the first EGFR-TKI received the approval by National Health Insurance issued by the Indonesian government. [27] Until the end of this study, there were no patients receiving afatinib as the first-line treatment that suffered from disease progression, and therefore, no plasma ctDNA examination done for these patients.

Among patients who had progressed after first-line gefitinib or erlotinib, our study detected 46.2% participants positive for T790M mutation. This result is comparable with the study conducted by Zheng et al., which found that the prevalence of T790M-positive mutation patients was 47%. In their study, the combination of T790M-positive mutation with either exon 19 deletion or exon 21 L858R mutation was found to be 29.3%, which is higher compared to single T790M mutation (17.9%). Unresult was in contrast to Socinski et al., which found that the prevalence of T790M mutation was 60%, aside from other types of non-EGFR mutations. This difference might be accounted to the difference in race and genetic factors between the Caucasian and Asian population. Further research is needed to confirm this assumption.

In our study, the proportion of patients with negative T790M mutation was 53.8%, in which 38.5% patients had no T790M mutation and 15.3% had no T790M mutation but were positive for either exon 19 deletion or exon 21 L858R mutation. This is consistent with Zheng et al., where the proportion of patients with negative T790M mutation but were positive for either exon 19 deletion or exon 21 L858R mutation was 6.5%-14.3%.[5] Based on the characteristics of patients, there were no significant differences between T790M positive and T790M negative mutation in terms of age, gender, smoking history, and EGFR-TKI treatment (P > 0.05). This is also consistent with the previous study by Zheng et al., which had the same findings.[5] Patients with positive T790M mutations from ctDNA test following EGFR-TKI are associated with poor prognosis. It could indicate that tumor cells have exceeded the threshold for tumor growth, and reflect an increase in tumor burden and also metastasis.[5]

PFS in this study was calculated from the time EGFR-TKI treatment was started until the earliest signs of disease progression assessed using RECIST version 1.1 and/or clinical worsening, Socinski et al. mentioned that resistance to EGFR-TKI will develop in patients after a median PFS of approximately 1-year (average 8-14 months).[13] In the current study, the median PFS was 9 months for both gefitinib and erlotinib. The result of our study is very similar to the WJTOG3405 study which asserted that the median PFS was 9.2 months. [28] Our previous study (thesis, unpublished data) found that the median PFS was 7 months,[27] while the IFUM study reported the median PFS of 9.7 months.[28] Twelve months survival rate in the current study was 36.1%, whereas in our previous study, it was 15.25%.[27] This might be due to immature data in our previous report.

In the current study, there was no difference in median PFS between the two types of EGFR-TKI treatment (gefitinib or erlotinib). The median PFS of gefitinib and erlotinib were 9 months, respectively (P = 0.932). In WJOG5108 L study comparing gefitinib and erlotinib, it was found that the median PFS for gefitinib was 8.3 months, while the median PFS for erlotinib was 10 months. [28]

There are several mechanisms of resistance to EGFR-TKI which result in disease progression. The T790M mutations are presumed to cause resistance to EGFR TKI through a variety of mechanisms. One of which is by steric hindrance, which results in the decrease of reversible TKI binding, increased bound affinity with ATP, and increased phosphorylation levels, which ultimately result in the decrease of EGFR-TKI potential. Other review suggests that the mutation causes changes in the tridimensional tyrosine kinase domain structure and prevents gefitinib or erlotinib from binding to EGFR.

CONCLUSIONS

In EGFR-mutated lung adenocarcinoma patients who had disease progression after the first-line EGFR-TKI, plasma ctDNA examination is a valid alternative method for tumor rebiopsy. Our study confirmed the conclusions of many other previous studies done in the same circumstances elsewhere. Using plasma ctDNA test in Dr. Soetomo General Hospital Surabaya, Indonesia, the proportion of T790M mutation in such patients was 46.2%. There were no significant differences between T790M-positive and T790M-negative mutations in terms of the age, sex, smoking history, and the type of EGFR-TKI used. Prior to the first-line EGFR-TKI treatment, EGFR common mutation in exon 19 and exon 21 was detected in 87.2% of the patients. The median PFS of patients receiving gefitinib or erlotinib as the first-line treatment was 9 months.

Acknowledgment

All authors would like to thank Ms. Roselini Ngiono B.Sc for manuscript proofread and her recommendations to improve our manuscript. The plasma ctDNA test was supported by AstraZeneca Ltd, Indonesia but it does not interferred in manuscript design and preparation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Dela Cruz CS, Tanoue LT, Matthay RA. Lung cancer: Epidemiology, etiology, and prevention. Clin Chest Med 2011;32:605-44.
- Ettinger DS, Wood DE, Akerley W, Bazhenova LA, Borghael H, Camidge DR, et al. Non-small cell lung cancer, version 6.2015. J Natl Compr Canc Netw 2015;13:515-24.
- Han B, Tjulandin S, Hagiwara K, Normanno N, Wulandari L, Laktionov K, et al. EGFR mutation prevalence in Asia-Pacific and Russian patients with advanced NSCLC of adenocarcinoma and non-adenocarcinoma histology: The IGNITE study. Lung Cancer 2017;113:37-44.
- Jenkins S, Yang JC, Ramalingam SS, Yu K, Patel S, Weston S, et al. Plasma ctDNA analysis for detection of the EGFR T790M mutation in patients with advanced non-small cell lung cancer. J Thorac Oncol 2017;12:1061-70.
- Zheng D, Ye X, Zhang MZ, Sun Y, Wang JY, Ni J, et al. Plasma EGFR T790M ctDNA status is associated with clinical outcome in advanced NSCLC patients with acquired EGFR-TKI resistance. Sci Rep 2016;6:20913.
- Wang Z, Cheng Y, An T, Gao H, Wang K, Zhou Q, et al. Detection of EGFR mutations in plasma circulating tumour DNA as a selection criterion for first-line gefitinib treatment in patients with advanced lung adenocarcinoma (BENEFIT): A phase 2, single-arm, multicentre clinical trial. Lancet Respir Med 2018;6:681-90.
- Seki Y, Fujiwara Y, Kohno T, Yoshida K, Goto Y, Horinouchi H, et al. Circulating cell-free plasma tumour DNA shows a higher incidence of EGFR mutations in patients with extrathoracic disease progression. ESMO Open 2018;3:e000292.
- Ishii H, Azuma K, Sakai K, Kawahara A, Yamada K, Tokito T, et al. Digital PCR analysis of plasma cell-free DNA for non-invasive detection of drug resistance mechanisms in EGFR mutant NSCLC: Correlation with paired tumor samples. Oncotarget 2015;6:30850-8.
- He C, Zheng L, Xu Y, Liu M, Li Y, Xu J. Highly sensitive and noninvasive detection of epidermal growth factor receptor T790M mutation in non-small cell lung cancer. Clin Chim Acta 2013;425:119-24.
- Metro G, Crino L. Advances on EGFR mutation for lung cancer. Transl Lung Cancer Res 2012;1:5-13.
- National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology (NCCN Guidelines). National Comprehensive Cancer Network Inc.; 2018.
- 12. Lindeman NI, Cagle PT, Aisner DL, Arcila ME, Beasley MB, Bernicker EH, et al. Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: Guideline from the College of American Pathologists, the International Association for the study of Lung Cancer, and the Association for Molecular Pathology. Arch Pathol Lab Med 2018;142:321-46.
- Socinski MA, Villaruz LC, Ross J. Understanding mechanisms of resistance in the epithelial growth factor receptor in non-small cell lung cancer and the role of biopsy at progression. Oncologist 2017;22:3-11.
- 14. Herbreteau G, Vallée A, Charpentier S, Normanno N, Hofman P.

- Denis MG. Circulating free tumor DNA in non-small cell lung cancer (NSCLC); Clinical application and future perspectives. J Thorac Dis 2019;11:S113-26.
- Lee JY, Qing X, Xiumin W, Yali B, Chi S, Bak SH, et al. Longitudinal monitoring of EGFR mutations in plasma predicts outcomes of NSCLC patients treated with EGFR TKIs: Korean lung cancer consortium (KLCC-12-02). Oncotarget 2016;7:6984-93.
- Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med 2009;361:947-57.
- Maemondo M, Inoue A, Kobayashi K, Sugawara S, Oizumi S, Isobe H, et al. Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. N Engl J Med 2010;362:2380-8.
- Sequist LV, Yang JC, Yamamoto N, O'Byrne K, Hirsh V, Mok T, et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. J Clin Oncol 2013;31:3327-34.
- Wu YL, Zhou C, Hu CP, Feng J, Lu S, Huang Y, et al. Afatinib versus cisplatin plus gemcitabine for first-line treatment of Asian patients with advanced non-small-cell lung cancer harbouring EGFR mutations (LUX-lung 6): An open-label, randomised phase 3 trial. Lancet Oncol 2014;15:213-22.
- Berols N, Touya D, Ubillos L, Bertoni B, Osinaga E, Varangot M. Prevalence of EGFR mutations in lung cancer in Uruguayan population. J Cancer Epidemiol 2017;2017:Article ID 6170290, https://doi. org/10.1155/2017/6170290.
- Sharma SV, Bell DW, Settleman J, Haber DA. Epidermal growth factor receptor mutations in lung cancer. Nat Rev Cancer 2007;7:169-81.
- Pirker R, Herth FJ, Kerr KM, Filipits M, Taron M, Gandara D, et al. Consensus for EGFR mutation testing in non-small cell lung cancer: Results from a European workshop. J Thorac Oncol 2010;5:1706-13.
- Wu JY, Wu SG, Yang CH, Gow CH, Chang YL, Yu CJ, et al. Lung cancer with epidermal growth factor receptor exon 20 mutations is associated with poor gefitinib treatment response. Clin Cancer Res 2008;14:4877-82.
- Noronha V, Choughule A, Patil VM, Joshi A, Kumar R, Susan Joy Philip D, et al. Epidermal growth factor receptor exon 20 mutation in lung cancer: Types, incidence, clinical features and impact on treatment. Onco Targets Ther 2017;10:2903-8.
- Mitsudomi T, Morita S, Yatabe Y, Negoro S, Okamoto I, Tsurutani J, et al. Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): An open label, randomised phase 3 trial. Lancet Oncol 2010:11:121-8.
- Inoue A, Kobayashi K, Maemondo M, Sugawara S, Oizumi S, Isobe H, et al. Updated overall survival results from a randomized phase III trial comparing gefitinib with carboplatin-paclitaxel for chemo-naive non-small cell lung cancer with sensitive EGFR gene mutations (NEJ002). Ann Oncol 2013;24:54-9.
- Fatmawati F. The profile of non-small cell lung cancer patients who
 received tyrosine-kinase inhibitors as first-line therapy in Dr. Soetomo
 General Academic Hospital, Surabaya. Indonesian language. [Thesis].
 Surabaya: Universitas Airlangga, 2016. Available form http://repository.
 unair.ac.id/id/eprint/39681.
- Douillard JY, Ostoros G, Cobo M, Ciuleanu T, McCormack R, Webster A, et al. First-line gefitinib in Caucasian EGFR mutation-positive NSCLC patients: A phase-IV, open-label, single-arm study. Br J Cancer 2014;110:55-62.
- Urata Y, Katakami N, Morita S, Kaji R, Yoshioka H, Seto T, et al. Randomized phase III study comparing gefitinib with erlotinib in patients with previously treated advanced lung adenocarcinoma: WJOG 5108L. J Clin Oncol 2016;34:3248-57.
- Cortot AB, Jänne PA. Molecular mechanisms of resistance in epidermal growth factor receptor-mutant lung adenocarcinomas. Eur Respir Rev 2014;23:356-66.





KOMITE ETIK PENELITIAN KESEHATAN RSUD Dr. SOETOMO SURABAYA

KETERANGAN KELAIKAN ETIK (" ETHICAL CLEARANCE ")

0632/KEPK/Ix/2018

KOMITE ETIK RSUD Dr. SOETOMO SURABAYA TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA PENELITIAN DENGAN JUDUL:

"Profil Mutasi T790M Pasien Kanker Paru Adenokarsinoma yang Mengalami Progresivitas Setelah Mendapatkan Inhibitor Tirosin Kinase Sebagai Terapi Lini Pertama dengan Pemeriksaan Circulating Tumor DNA"

PENELITI UTAMA: Dr. Laksmi Wulandari, dr., Sp.P (K), FCCP

PENELITI LAIN: 1. Vinodini Merinda, dr

UNIT / LEMBAGA / TEMPAT PENELITIAN: RSUD Dr. Soetomo

DINYATAKAN LAIK ETIK

Berlaku dari : 16/09/2018 s.d 16/09/2019 Surabaya, 16 September 2018

KETUA

(Dr. Elizeus Hanindito, dr., Sp.An, KIC,KAP) NIP. 19511007 197903 1 002

*) Sertifikat ini dinyatakan sah apabila telah mendapatkan stempel asli dari Komite Etik Penelitian Kesehatan

Source details

Scopus Preview



CiteScore CiteScore rank & trend Scopus content coverage

Improved CiteScore methodology CiteScore 2020 counts the citations received in 2017-2020 to articles, reviews, conference papers, book chapters and data papers published in 2017-2020, and divides this by the number of publications published in 2017-2020. Learn more >

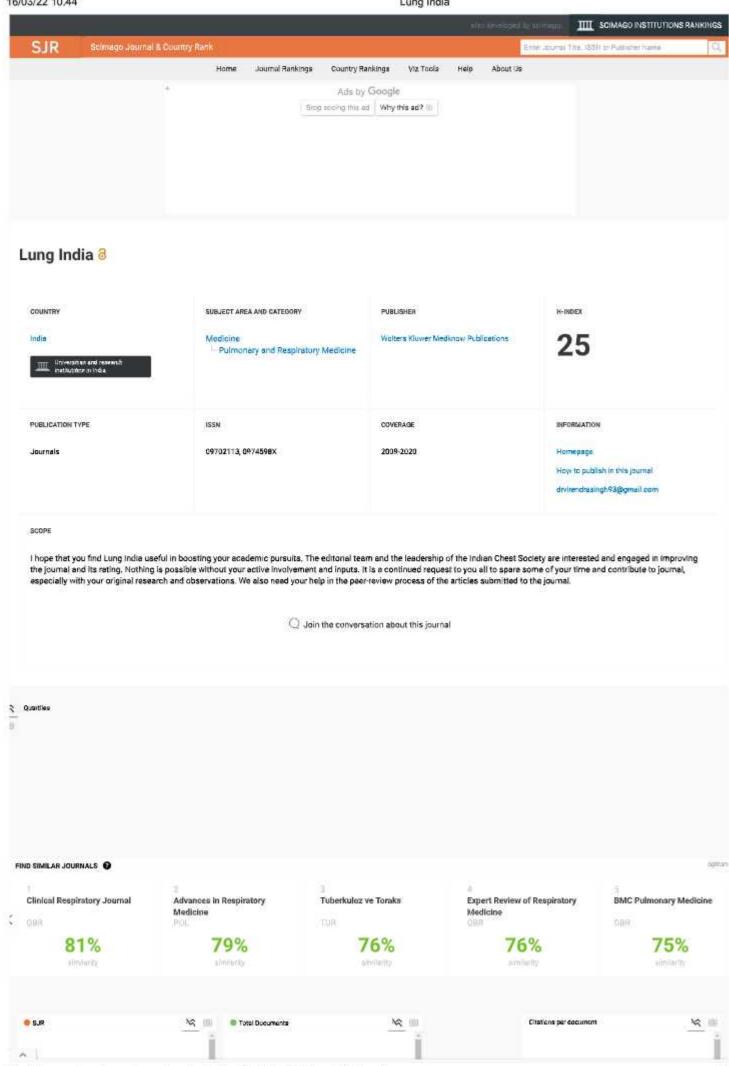


CiteScore rank 2020 @

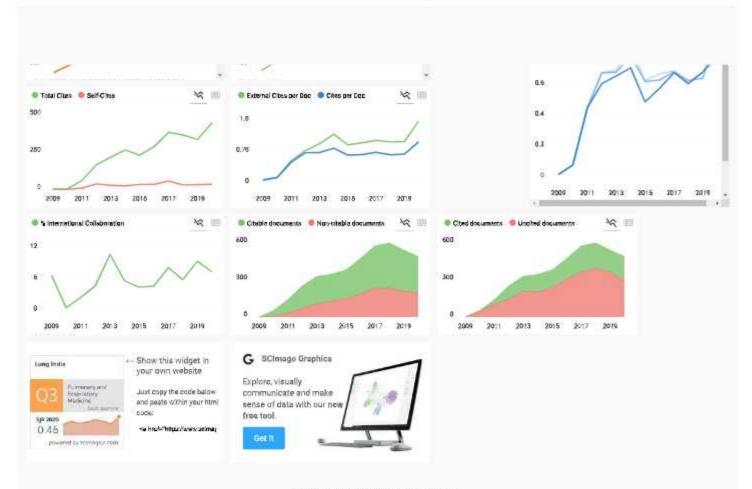
Category	Rank	Percentile
Medicine		
 Pulmonary and Respiratory 	#84/133	37th
Medicine		

View CiteScore methodology > CiteScore FAQ > Add CiteScore to your site &

16/03/22 10.44 Lung India



16/03/22 10.44 Lung India



Metrics based on Scopus@ data as of April 2021

