

EXPERIENCE
BRINGS

Confidence

 **Tarceva**
erlotinib



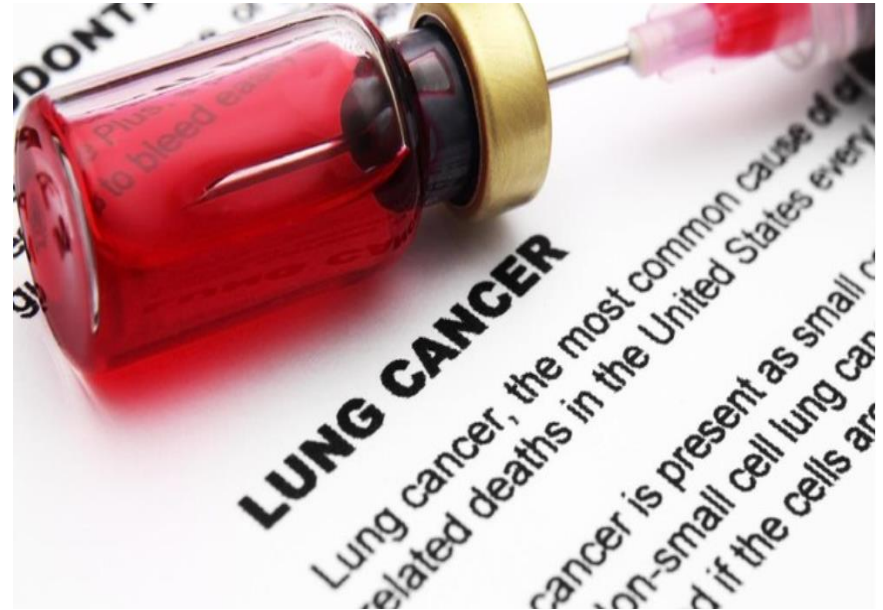
Exposure to Air Pollution and Pollutant as a
Trigger Factor for the causes of Lung Cancer

Dr dr Harun Iskandar Sp. P(K)

Departemen Pulmonologi & Kedokteran Respirasi

Umur Warga Indonesia Bisa 'Hilang' Lima Tahun Disebabkan Paparan Polusi dan Lingkungan

- Kabar duka datang dari aktor komedi senior Indonesia, **Indro Warkop** yang baru saja di 2018 kehilangan istrinya, akibat **kanker paru**.
- Sebelumnya, di 2012 mantan menteri kesehatan, Dr Endang Rahayu juga meninggal karena kanker paru
- Jenis kanker paru yang hingga kini juga masih menggerogoti Kepala Pusat Data dan Humas BNPB (Badan Nasional Penanggulangan Bencana) Sutopo PN.
- Ketiga kasus ini memberi pelajaran, kanker paru tak melulu terjadi pada perokok aktif.



Paparan Polusi Udara & Polutan Faktor Penyebab Kanker Paru

- Salah satu faktor risiko terbesar kanker paru adalah polusi udara, yang datang dari rokok dan aktivitas manusia setiap hari.
- Level polusi dan bahaya rokok sama terkait kanker paru. Riset menemukan, peningkatan tiap 10 mikrogram per kubik konsentrasi materi polusi dalam tubuh, memperbesar risiko kematian akibat kanker paru sebesar 27 %.
- Responden dalam riset ini adalah orang yang tidak merokok.
- Risiko tersebut mungkin lebih besar pada kota megapolitan seperti Jakarta, New Delhi, dan Beijing. Negara berkembang umumnya berbagi risiko karena masih minim infrastruktur terkait kebersihan udara.
- Masyarakat di kota tersebut harus menghirup udara yang tercampur asap kendaraan, pabrik, rumah tangga, dan peralatan pembangunan

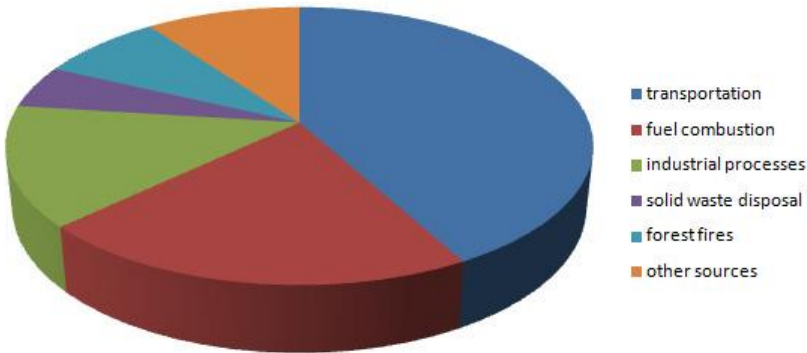


Paparan Polusi Udara & Polutan Faktor Penyebab Kanker Paru

- Berdasarkan data internasional, sekitar 3-5 % penderita kanker paru berhubungan dengan pajanan polusi udara. Bahkan, data hasil penelitian di RSUP Persahabatan pada 2013 terhadap 300 penderita kanker paru yang terbukti sebanyak 4 % pasien terpapar polusi udara.
- Saat ini salah satu yang menjadi pembahasan oleh Organisasi Kesehatan Dunia (WHO) bahwa kanker bisa muncul karena dampak dari polusi udara.
- Polutan yang paling berpengaruh terhadap penyakit kanker ialah partikulat matter (PM) 2,5 atau partikel halus dengan ukuran di bawah 2,5 mikron yang bisa masuk ke dalam organ-organ dalam tubuh manusia.
- PM 2,5 kalau terhirup dari saluran napas, selama kontinyu akan merangsang terjadinya perubahan sel yang ada di dalam saluran napas dan paru-paru dari yang normal menjadi abnormal, dan terjadilah kanker.

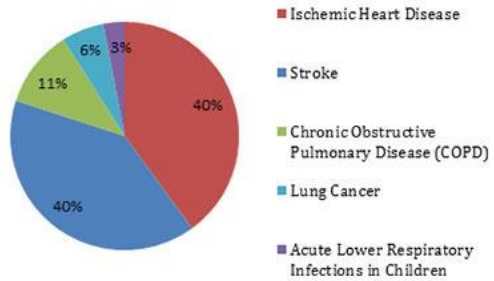


major sources of air pollution

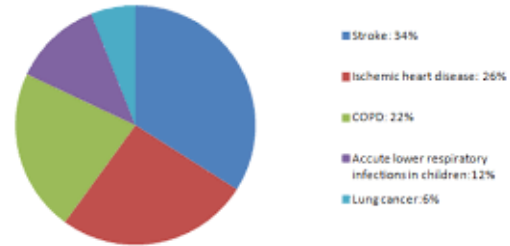




Ambient Air Pollution



Indoor air pollution-caused deaths – breakdown by disease



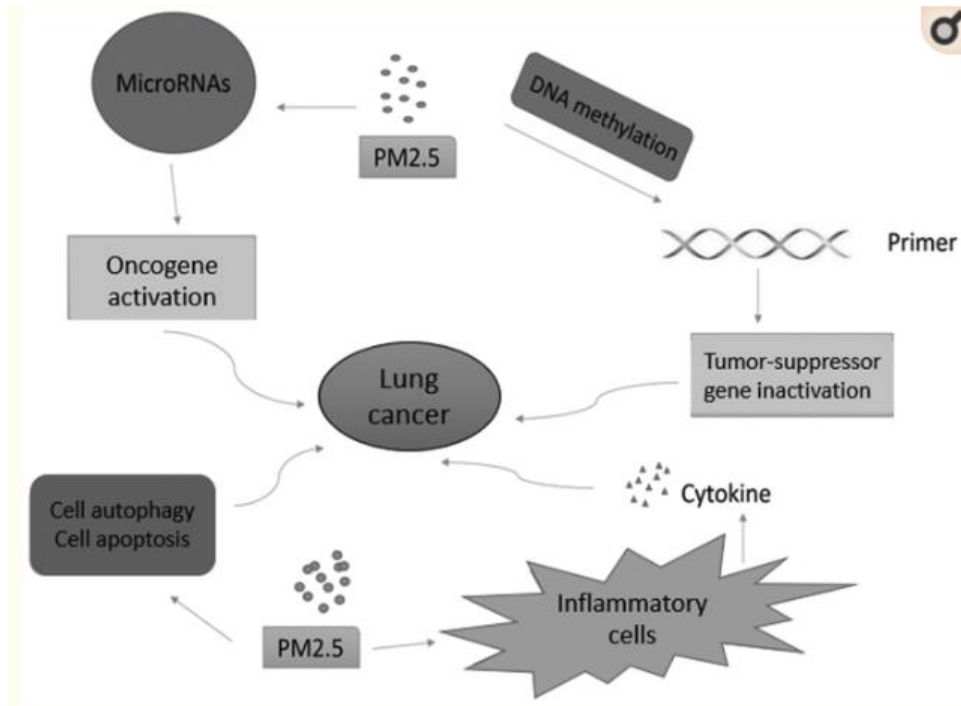


Figure 1.

Function of PM2.5 in the pathogenesis of lung cancer. PM2.5 induces oncogene activation and tumor suppressor gene inactivation through microRNA dysregulation and DNA methylation in lung cancer. Tumor microenvironment alteration is also detected in PM2.5-induced inflammatory cells. PM2.5, particulate matter 2.5.

Air Pollution Exposures based on Stages at Diagnosis of Lung Cancer

Air pollution exposures (Mean ± SD or %)	Localized Only (n=59,609)	Regional (n=73,513)	Distant Site(s) (n=186,496)	Unknown (n=32,435)	Total (n=352,053)
NO ₂ (ppb)	20.6 ± 9.3	21.4 ± 9.7	22.0 ± 10.4	24.5 ± 11.3	21.9 ± 10.2
% available ^a	87.6	86.8	87.3	83.0	86.8
O ₃ (ppb)	40.3 ± 9.7	40.3 ± 10.8	40.0 ± 12.8	41.2 ± 12.8	40.2 ± 11.9
% available ^a	93.6	93.2	93.3	89.9	93.0
PM ₁₀ (µg/m ³)	30.5 ± 10.7	31.4 ± 11.6	31.9 ± 12.4	35.0 ± 13.5	31.8 ± 12.1
% available ^a	91.7	91.3	91.4	88.6	91.2
PM _{2.5} (µg/m ³) ^b	13.0 ± 4.5	13.4 ± 4.9	13.9 ± 5.6	14.6 ± 5.7	13.7 ± 5.3
% available ^a	86.5	84.3	82.6	76.8	83.3

Median Survival and 5-Year Survival Rate, by stage at diagnosis and air pollution exposure

Categorized air pollution exposure	Median survival (years)			Five-year survival rate (%) ^a		
	Localized	Regional	Distant	Localized	Regional	Distant
NO₂ (ppb)						
< 14	5.4	1.6	0.3	50	24	4
14 – 20.5	4.2	1.4	0.4	45	21	4
20.5 – 27	3.2	1.2	0.4	38	17	3
≥ 27	2.2	1.0	0.3	30	12	2
O₃ (ppb)						
< 32	2.8	1.0	0.3	36	16	2
32 – 39.5	3.8	1.4	0.5	42	19	3
39.5 – 47	4.9	1.6	0.5	49	23	4
≥ 47	2.7	1.1	0.3	35	15	2
PM₁₀ (µg/m³)						
< 23	4.7	1.5	0.3	47	23	4
23 – 30.5	4.4	1.4	0.4	45	20	4
30.5 – 38	3.7	1.3	0.4	43	19	3
≥ 38	2.1	1.0	0.3	27	11	2
PM_{2.5} (µg/m³)^b						
< 10	5.7	1.9	0.3	51	27	4
10 – 13	5.0	1.9	0.5	48	25	5
13 – 16	4.5	1.5	0.5	46	23	4
≥ 16	2.4	1.2	0.3	31	14	2

Paparan Asap Rokok Faktor Penyebab Kanker Paru

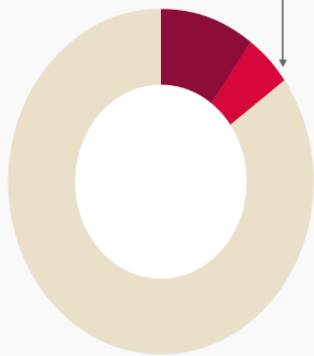
- Rokok saat ini memang masih jadi faktor risiko terbesar kanker paru. Namun efek yang ditimbulkan cenderung bersifat personal, sedangkan paparan asap dan polusi mampu menjangkau lebih banyak orang
- Sebanyak 15 % kanker paru ternyata terjadi pada orang yang tidak merokok.
- Usaha preventif sedini mungkin untuk mencegah risiko kanker paru. Salah satunya dengan penggunaan masker, menjaga pola makan, tidak merokok, dan olahraga.



Incidence of EGFR mutation-positive tumours in NSCLC patients

10%-15%

EGFR mutation-positive NSCLC ¹



Approximately **90%**
of those mutations
are exon 19 deletions
and exon 21 (L858R)
substitutions ²

In Asian populations around
around 50%
of NSCLC tumours are EGFR
mutation positive ³



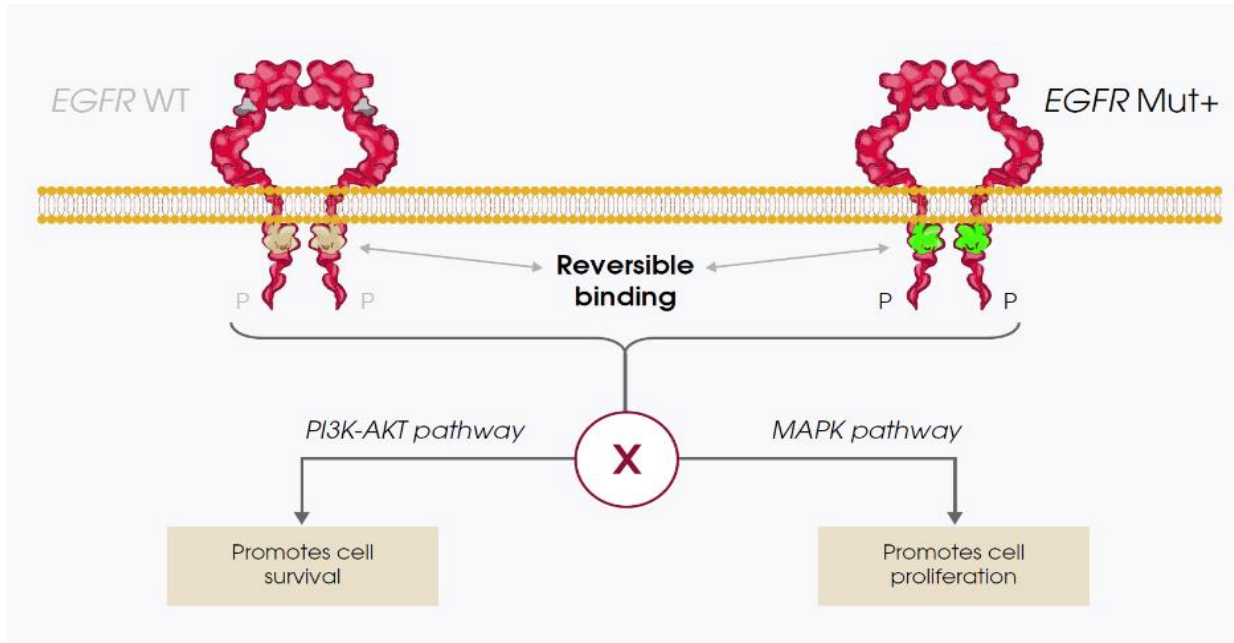
1. Krawczyk et al. Oncol Lett. 2017;13(6):4433-4444
2. Lindeman et al. J Thorac Oncol. 2013;8(7):823-59
3. Shi et al. J Thorac Oncol. 2014; 9(2): 154-162



Mechanism Of Action

EGFR mutation-positive tumours are hyper-dependent on EGFR signalling for their survival^{1,2}

Inhibiting the activity of EGFR and its signalling prevents the proliferation and survival of EGFR mutation-positive NSCLC¹



1. Soria et al. Cancer Treat Rev. 2012;38(5):416-30

2. Chong et al. Nat Med. 2013;19(11):1389-1400





- Est. 2019 -
ALK+
Alectinib

ENTRK

ROS-1

- Now -
EGFR Mut+ and EGFR Wild Type

 **Tarceva**[®]
erlotinib
Breathe.Fight.

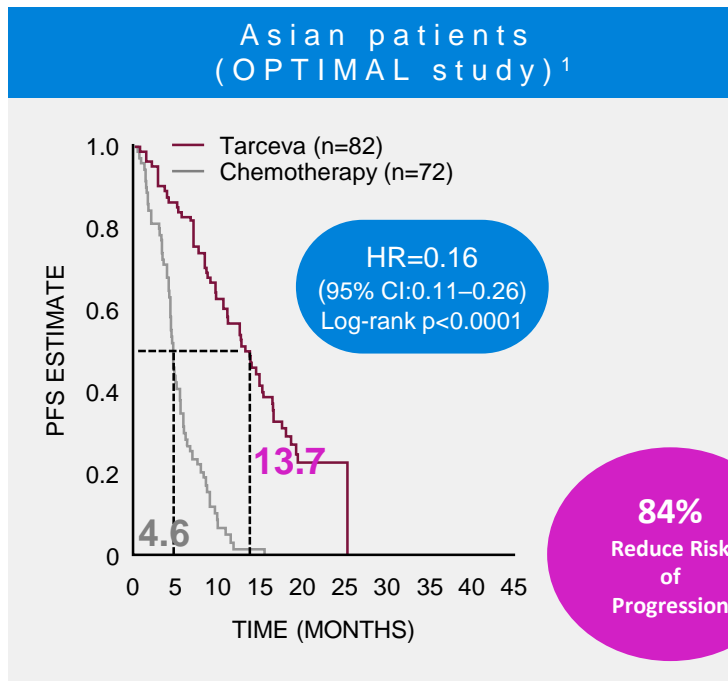
 **AVASTIN**[®]
bevacizumab

 **TECENTRIQ**[™]
atezolizumab INJECTION FOR
INTRAVENOUS USE 1200 mg
- 2019 -
Anti PDL1

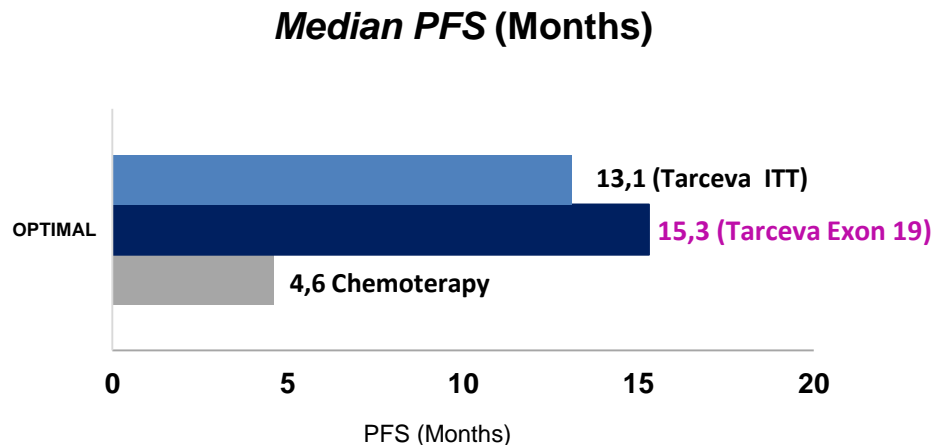




First-line treatment with Tarceva provides above 1 year (13.7 months) of survival in EGFR Mut+ advanced NSCLC



Tarceva provides PFS of 15,3 Months in sub-patients in Exon 19 Deletion¹



ITT = intention-to-treat.



PLOS One 2016 : Meta-Analysis of Efficacy & Safety of 3 EGFR TKIs¹

- **Meta-Analysis of 3 EGFR TKIs**
- **16 of Phase III Trials**
- **With 2,962 patient cases of EGFR Mut+**

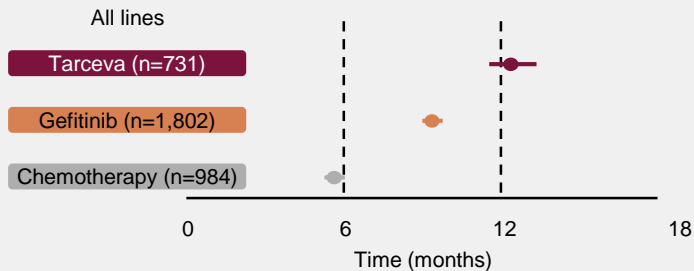
	Efficacy	Safety
Erlotinib	High	Moderate
Gefitinib	Moderate	Moderate
Afatinib	High	High

1. Optimized selection of three major EGFR-TKIs in advanced EGFR-positive non-small cell lung cancer: a network meta-analysis by Yaxiong Zhang

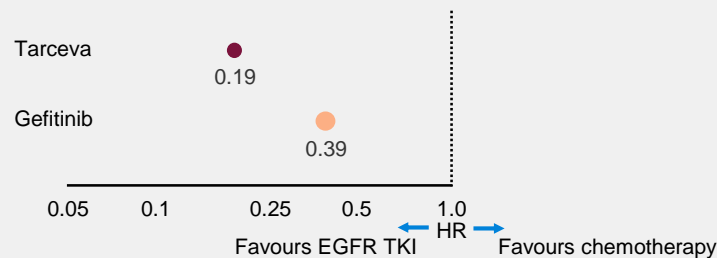


Tarceva provides a similar or higher PFS benefit versus chemotherapy than gefitinib or afatinib in different meta-analyses

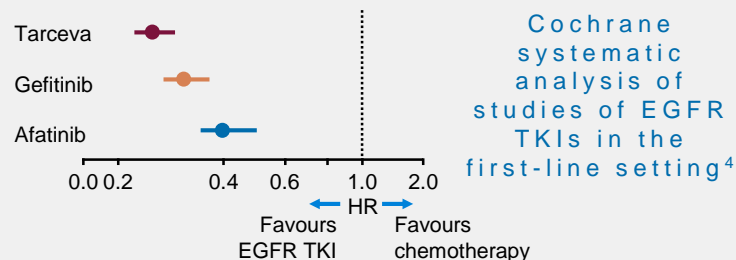
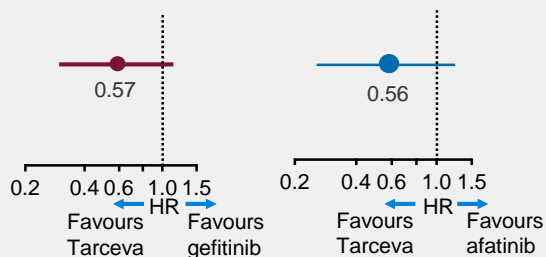
A pooled analysis of data from >90 published studies¹



A meta-analysis of patients in 9 randomised, controlled trials²



A network analysis of data from phase III clinical trials³



Cochrane systematic analysis of studies of EGFR TKIs in the first-line setting⁴

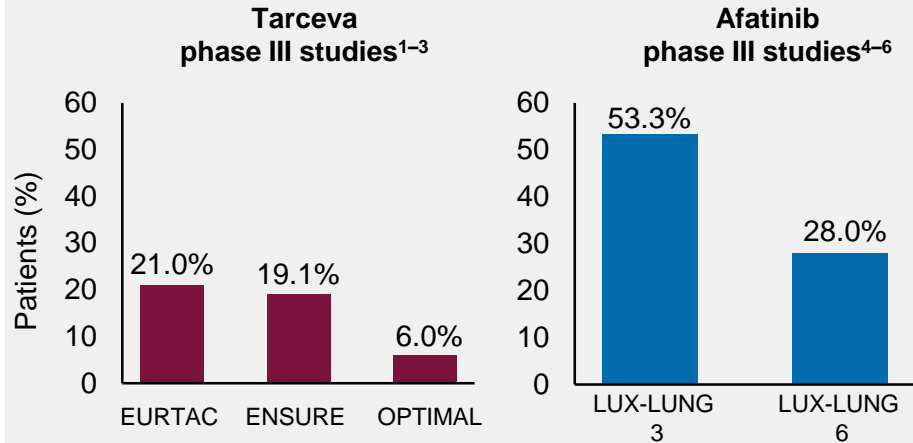
1. Paz-Ares, et al. J Cell Mol Med 2014; 2. Petrelli, et al. Clin Lung Cancer 2012
3. Haaland, et al. J Thorac Oncol 2014; 4. Greenhalgh, et al. Cochrane Database of Systematic Reviews 2016





Tarceva has a favourable safety profile, with lower rates of dose reductions and treatment discontinuations compared with second-generation EGFR TKIs

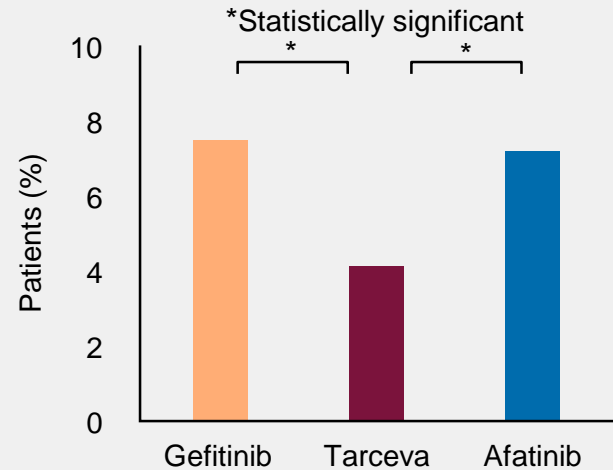
Dose Reductions



Dose reductions due to AEs were required by up to **21%** of patients treated with Tarceva¹⁻³

Afatinib dose reductions due to AEs were required by up to **57%** of patients⁷

Treatment Discontinuations⁸



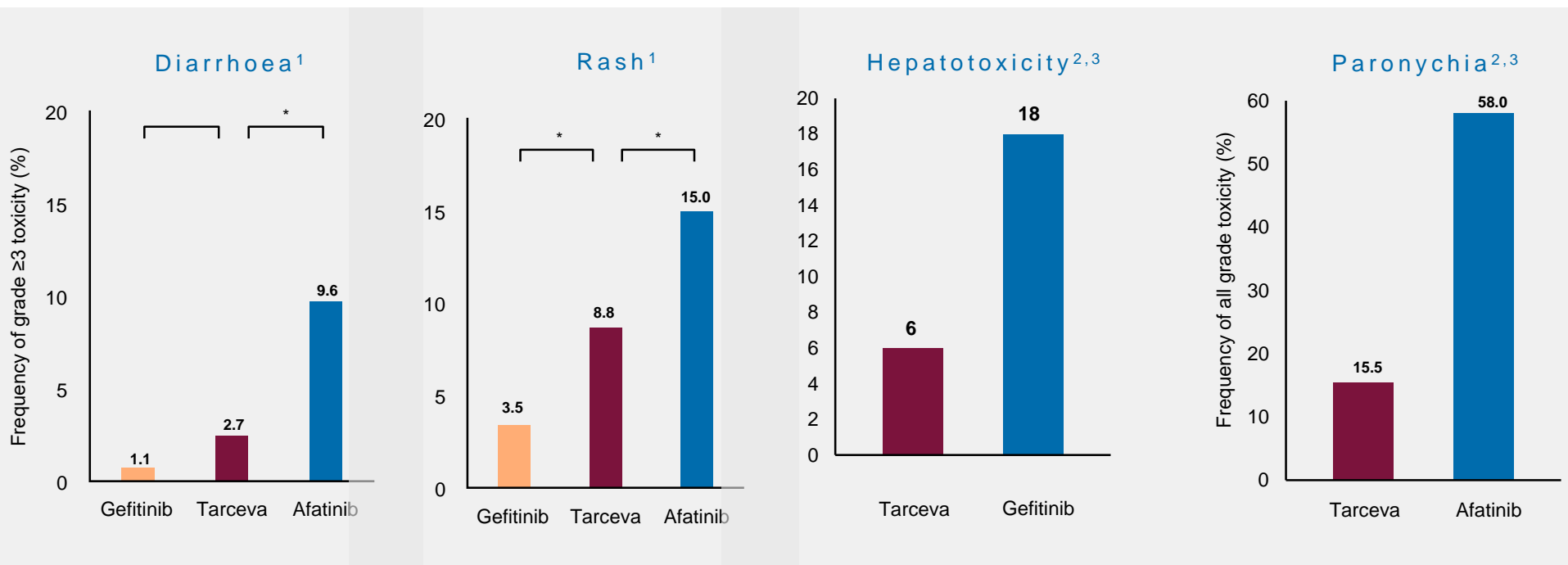
1. Rosell, et al. Lancet Oncol 2012; 2. Wu, et al. Ann Oncol 2015; 3. Zhou, et al. Lancet Oncol 2011; 4. Sequist, et al. J Clin Oncol 2013; 5. Yang, et al. Ann Oncol 2016; 6. Wu, et al. Lancet Oncol 2014; 7. Gilotrif SmPC; 8. Takeda, et al. Lung Cancer 2015
AE = adverse event; TKIs = tyrosine kinase inhibitors





Incidence of rash, diarrhoea, paronychia are lower with Tarceva than with second-generation TKIs

Hepatotoxicity are lower with Tarceva than with other first-generation TKI



A pooled analysis of data from 22 published phase II and III clinical studies¹

Data from phase III Tarceva study and afatinib SmPC^{2,3}



*Statistically significant

SmPC = summary of product characteristics

1. Takeda, et al. Lung Cancer 2015; 2. Wu, et al. Ann Oncol 2015; 3. Gilotrif SmPC



Management of Skin Rash of Tarceva¹

	Tarceva Dose	Topical Therapy	Systemic Therapy
Mild (Stage 1)	Maintained	Steroid Antibiotic	-
Moderate (Stage 2)	Maintained	Steroid Antibiotic	Antibiotic
Severe (Stage 3–4)	Recommended of dose reduction and/or discontinue	Steroid Antibiotic	Antibiotic Corticosteroid

Re-evaluation of every 2 weeks

1. Lynch, T., Kim, E. & Eaby, B. (2007). Epidermal Growth Factor Receptor Inhibitor–Associated Cutaneous Toxicities: An Evolving Paradigm in Clinical Management. *The Oncologist* 12:610-621. Retrieved from www.theoncologist.com (on April 26, 2016)

Dosing & Administration Tarceva¹

Dosing :

- Oral (2 Strengths – 150 mg & 100 mg)
- The recommended daily dose of Tarceva is 150mg
- Recommended of dose reduction in adverse events of grade 3 – 4

Administration :

- Tarceva should be taken on an empty stomach
- At least 1 hour before or 2 hours after the ingestion of food



Summary

- Polusi udara factor risiko kanker paru
- Polutan yang paling berpengaruh terhadap penyakit kanker ialah particulat matter (PM) 2,5 atau partikel halus dengan ukuran di bawah 2,5 mikron yang bisa masuk ke dalam organ-organ dalam tubuh manusia
- Mekanisma air polutan menyebabkan kanker paru adalah menginduksi onkogen dan inaktivasi tumor suppressor

EXPERIENCE
BRINGS **Confidence**



Tarceva provides EGFRmut+ patients an optimal balance of efficacy and safety compared with other first-/ second-generation EGFR TKIs¹⁻⁴

1. Zhang Y, et al. Oncotarget. Vol. 7, No. 15 (2016)
2. Zhou C, et al. Lancet Oncol. 12: 735-42 (2011)
3. Takeda M, et al. Lung Cancer. 88 : 74-79 (2015)
4. BPOM Product Information Tarceva (Erlotinib) December 2018

THANK YOU

Do you have any question or literature request on Roche product or their associated therapeutic areas



Ask
MI!

Roche Indonesia
Medical Information (MI) Service

E-mail : jakarta.medical_information@roche.com

Phone : 0800 140 1578 (Toll Free)

ADVERSE EVENT REPORTING

Adverse Event (AE)

Any **untoward medical occurrence** in a patient or clinical investigation subject administered a pharmaceutical drug and **which does not necessarily have a causal relationship with this treatment.**

Example: any unfavorable and unintended sign and symptom (including an abnormal laboratory finding), and pregnancy.

REPORTING ADVERSE EVENT IS MANDATORY ACCORDING TO INDONESIAN REGULATORY AUTHORITY (REGULATION HEAD OF BPOM RI No HK.03.1.23.11.10690 Year 2011 ON PHARMACOVIGILANCE IMPLEMENTATION BY PHARMACEUTICALS)

If you are aware of any AE pertaining to Roche product, please report to:

Local Safety Unit
PT Roche Indonesia



0-800-140-1579 (toll-free)



indonesia.safety@roche.com



021 2253 2720

All the data collected will be used for drug monitoring purpose only