



Post-ASCO 2018

Lungekræft



Junior speaker: Jakob Sidenius Johansen, reservelæge, klinisk assistent

Senior speaker: Gitte Persson, overlæge, ph.d.

Herlev Hospital, Onkologisk Afdeling R, Lunge Team



Disclosures

Lungecancer Lidt statistikker

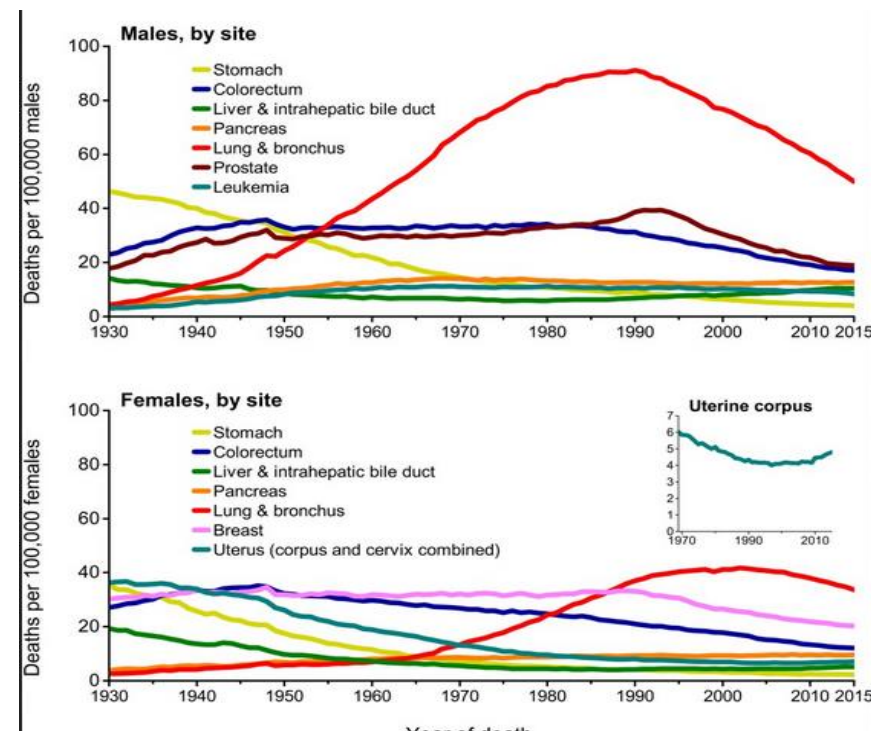
Estimated New Cases				
	Males		Females	
Prostate	164,690	19%	Breast	266,120 3
Lung & bronchus	121,080	14%	Lung & bronchus	112,350 1
Colon & rectum	75,610 9%		Colon & rectum	64,640
Urinary bladder	62,380 7%		Uterine corpus	63,230
Melanoma of the skin	55,150 6%		Thyroid	40,900
Kidney & renal pelvis	42,680 5%		Melanoma of the skin	36,120
Non-Hodgkin lymphoma	41,730 5%		Non-Hodgkin lymphoma	32,950
Oral cavity & pharynx	37,160 4%		Pancreas	26,240
Leukemia	35,030 4%		Leukemia	25,270
Liver & intrahepatic bile duct	30,610 4%		Kidney & renal pelvis	22,660
All Sites	856,370	100%	All Sites	878,980 10

Estimated Deaths				
	Males		Females	
Lung & bronchus	83,550	26%	Lung & bronchus	70,500 2
Prostate	25,400 8%		Breast	46,920 1
Colon & rectum	27,390 8%		Colon & rectum	23,240
Pancreas	23,020 7%		Pancreas	21,310
Liver & intrahepatic bile duct	20,540 6%		Ovary	14,070
Leukemia	14,270 4%		Uterine corpus	11,350
Esophagus	12,850 4%		Leukemia	10,100
Urinary bladder	12,520 4%		Liver & intrahepatic bile duct	9,660
Non-Hodgkin lymphoma	11,510 4%		Non-Hodgkin lymphoma	8,400
Kidney & renal pelvis	10,010 3%		Brain & other nervous system	7,340
All Sites	323,630	100%	All Sites	286,010 10

4.600 nye tilfælde årligt i DK, 1,8 mill. i verden

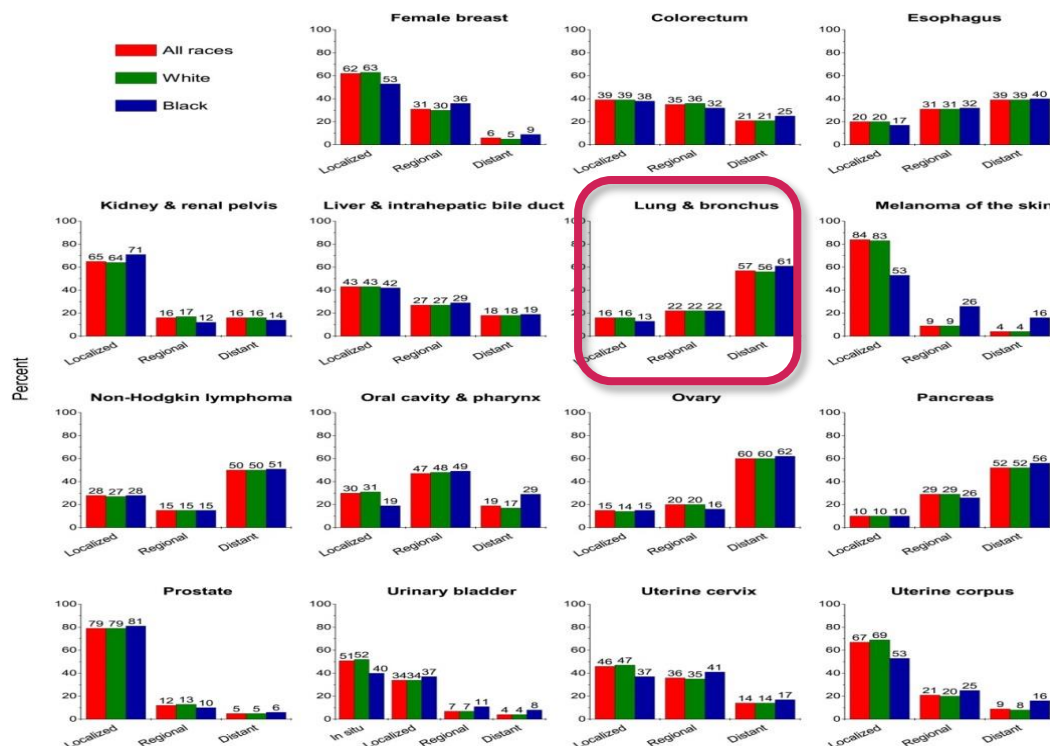
Hyppigste årsag til kræftdødsfald i DK og i verden

Primære årsag er tobaksrygning



Trends i Cancer dødsårsag, USA, 1930-2015

Behandlingsstrategier Ny vin på nye og gamle flasker

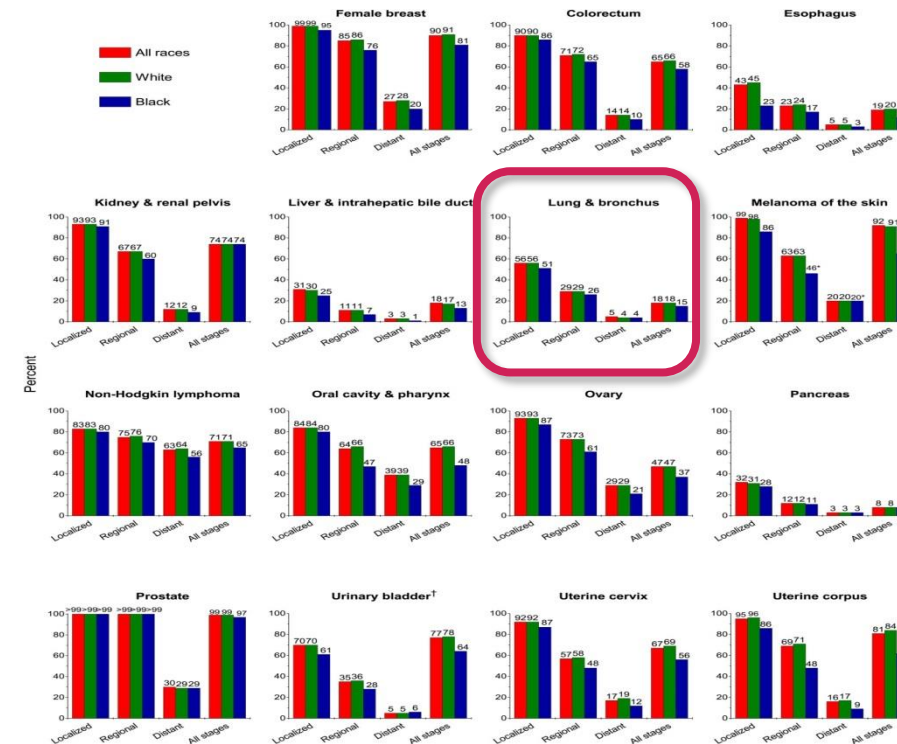
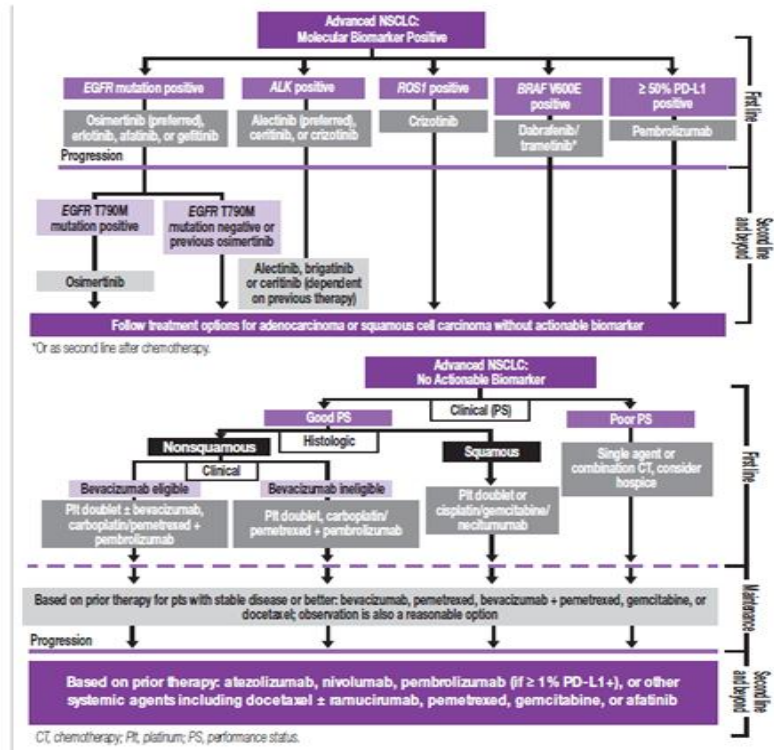


Stadie	Behandling	Overlevelse (5 år)
I	Kirurgi stereotaktisk stråleterapi	77-92%*
II	Kirurgi + adjuverende kemoterapi	53-60%*
III	Konkomitant kemoradioterapi	13-36%*
IV	Immunoterapi Kemoterapi Måltet terapi Stråleterapi	0-10%*

*Detterbeck et al. J Thor Oncol, 11 (9) (2016), pp. 1433-1446

Stadiedistribution, USA, 2007-2013

Behandlingsmodaliteter

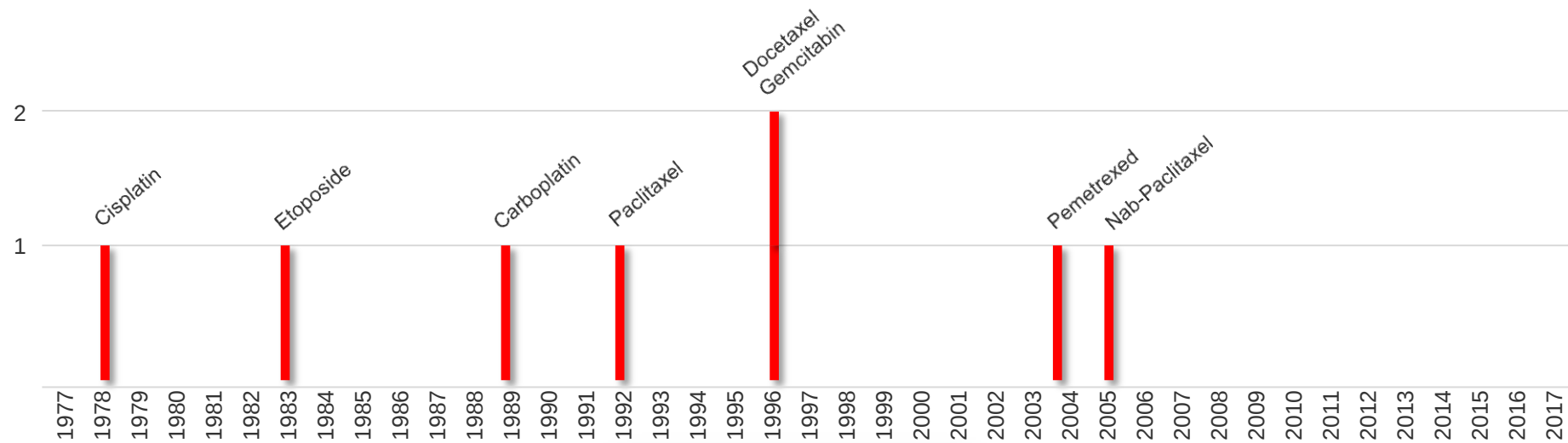


Komplekse behandlingsalgoritmer

5-års overlevelse og baseline stadie, USA, 2007-2013 (Obs, inden IO)



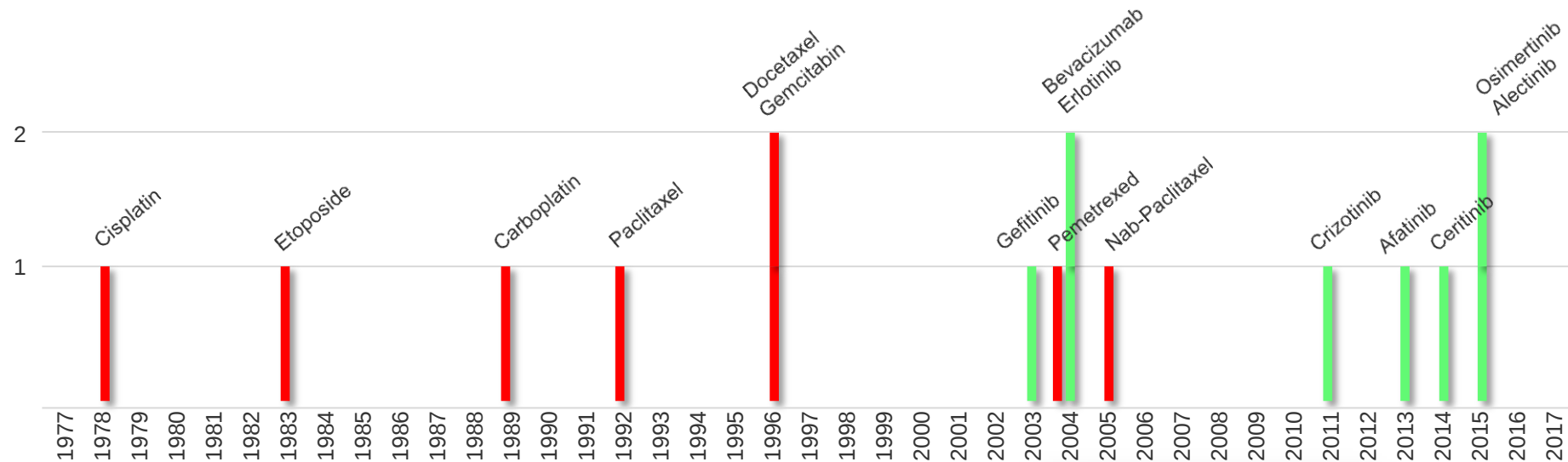
Kemoterapi, et maraton (1978 – 2005)



Kemoterapi



Targeteret behandling, et 3.000 m forhindringsløb (2003-2015)



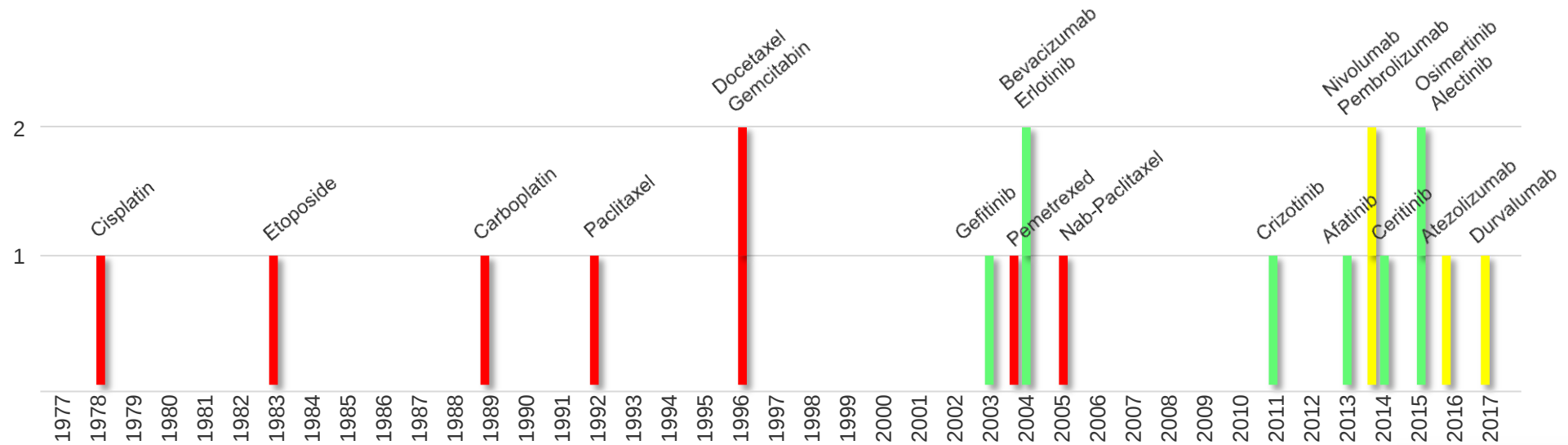
Kemoterapi



Targeteret
behandling
(ALKi, EGFR-TKI,
VEGFi)



Immunterapi, en 100 m sprint (2014-2017)



Kemoterapi



Targeteret
behandling
(ALKi, EGFR-TKI,
VEGFi)



Immunterapi





Lungecancer studier, ASCO 2018

Udvælgelseskriterier

Fase 3

Primære endpoint: OS

Sekundært endpoint: Safety (QoL)

Klinisk relevant

1. Keynote-042 (Pembrolizumab)

NSCLC, PD-L1 >1%, 1.L, IO-mono, F3

2. NEJ009 (Gefitinib + Platin/Pemetrexed)

NSCLC, EGFR-mut, 1.L, TT + KT-kombi, F3

3. Baseline Steroids, Review

NSCLC, Retrospektivt, 2-center, Register

4. Fremtidens højdespringere?



Keynote-042 (Pembrolizumab) Fase 3, 1. linje til metastatisk NSCLC

Pembrolizumab vs Platinum-Based Chemotherapy as First-Line Therapy for Advanced/Metastatic NSCLC With a PD-L1 TPS $\geq 1\%$: Open-Label, Phase 3 KEYNOTE-042 Study

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Igor Bondarenko,¹⁰ Karou Kubota,¹¹ Gregory M Lubiniecki,¹² Jin Zhang,¹² Debra Kush,¹²
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Pembrolizumab and PD-L1 for Metastatic NSCLC

- Monotherapy significantly improved OS vs docetaxel in metastatic NSCLC of PD-L1 tumor proportion score (TPS) $\geq 1\%$ that progressed on or after platinum-containing chemotherapy^{1a}
- Monotherapy significantly improved PFS and OS vs platinum-based chemotherapy in previously untreated metastatic NSCLC with PD-L1 TPS $\geq 50\%$ ^{2b}
- Combination with platinum-based chemotherapy significantly improved OS over chemotherapy alone in untreated metastatic NSCLC, irrespective of PD-L1 expression^{3,4b}
- Companion diagnostic: PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies)
 - Used to assesses PD-L1 expression in formalin-fixed tumor samples
 - Expression measure: TPS, defined as the percentage of tumor cells with membranous PD-L1 staining

^aPts with sensitizing EGFR or ALK alteration must have also progressed on an appropriate TKI. ^bPts with sensitizing EGFR or ALK alteration were excluded.
1. Herbst RS et al. *Lancet* 2016;387:1540-50. 2. Reck M et al. *N Engl J Med* 2016;375:1823-33.
3. Gandhi L et al. *N Engl J Med* 2018;378:2078-92. 4. Paz-Ares L et al. Presented at ASCO 2018; abstract 105.

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KN-010: 2.L mono, IO, F3

KN-024: 1.L mono, IO, F3 -> st. 1.L Pembro

KN-189: 1.L kombi, IO, F3

Keynote-042 (Pembrolizumab) Fase 3, 1. linje til metastatisk NSCLC

First-Line Pembrolizumab Monotherapy

- KEYNOTE-024: pembrolizumab monotherapy vs platinum-based chemotherapy for metastatic NSCLC with PD-L1 TPS $\geq 50\%$ and no sensitizing *EGFR* or *ALK* alterations¹
 - Pembrolizumab provided superior PFS (primary end point) and OS (key secondary end point)
 - Pembrolizumab had a better safety profile

- Unmet need: more effective and tolerable first-line therapy for metastatic NSCLC

Objective of KEYNOTE-042 (NCT02228094): investigate role of first-line pembrolizumab in patients with PD-L1 expression (TPS $\geq 1\%$)

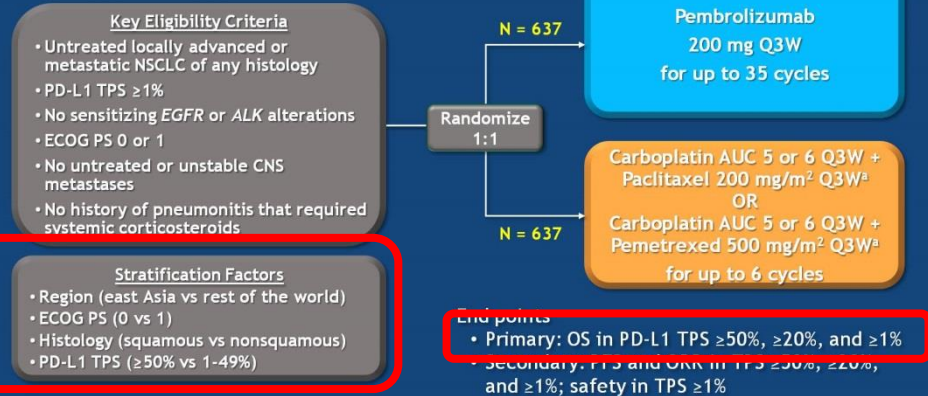
1. Reck M et al. *N Engl J Med* 2016;375:1823-33.

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KEYNOTE-042 Study Design



¹Pemetrexed maintenance therapy was optional but strongly encouraged for patients with nonsquamous histology.

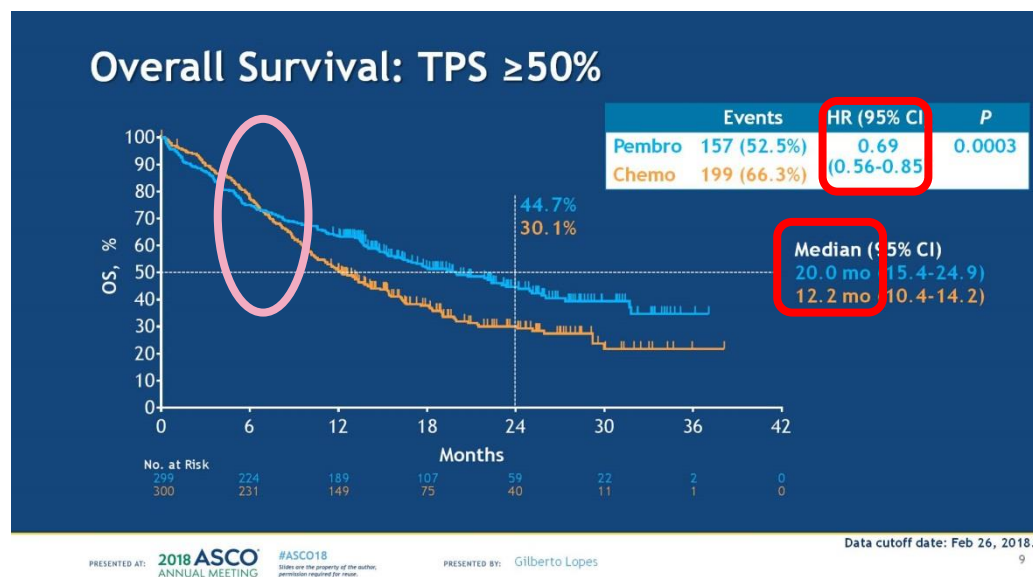
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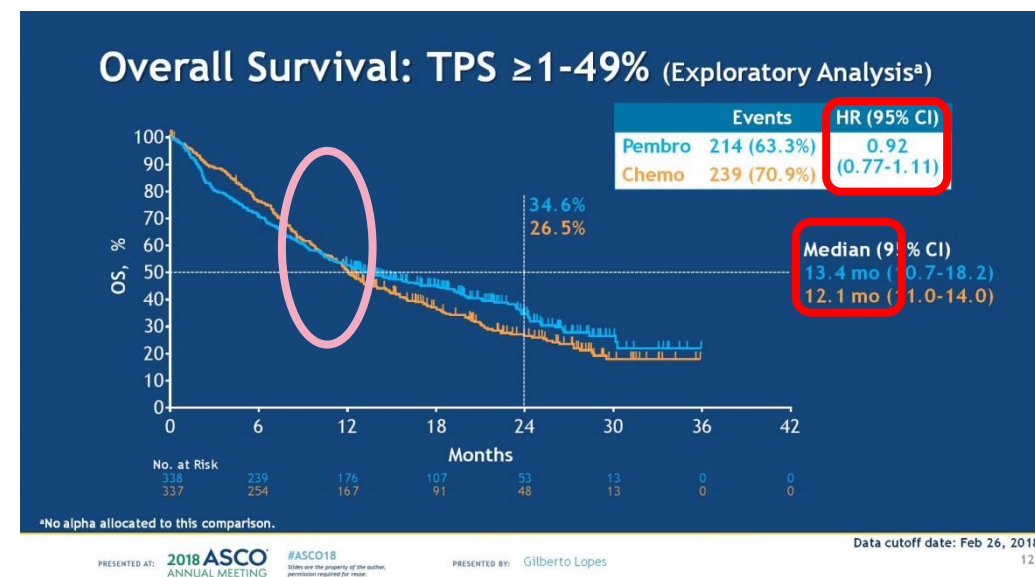
4

KN-024: fase 3, 1.linje mono IO

Keynote-042 (Pembrolizumab) Fase 3, 1. linje til metastatisk NSCLC



*Hvorfor krydser kurverne først efter 6 mdr?
Hvem har ikke gavn af IO?*



*One-size doesn't fit all!
De høje TPS løfter kurven.*

Keynote-042 (Pembrolizumab) Fase 3, pallierende 1. linie Immun-monoterapi

Summary of Exposure and Adverse Events: All Treated Patients

	Pembrolizumab (N = 636)	Chemotherapy (N = 615)
No. of doses, median (range)	9 (1-36)	6 (1-42)
Treatment-related AEs	399 (62.7%)	553 (89.9%)
Grade 3-5	113 (17.8%)	252 (41.0%)
Led to death	13 (2.0%)	14 (2.3%)
Led to discontinuation	57 (9.0%)	58 (9.4%)
Immune mediated AEs and infusion reactions ^a	177 (27.8%)	44 (7.2%)
Grade 3-5	51 (8.0%)	9 (1.5%)
Led to death	1 (0.2%) ^b	0

^aBased on a list of terms specified by the sponsor and considered regardless of attribution to treatment or immune relatedness by the investigator.

^bPneumonitis.

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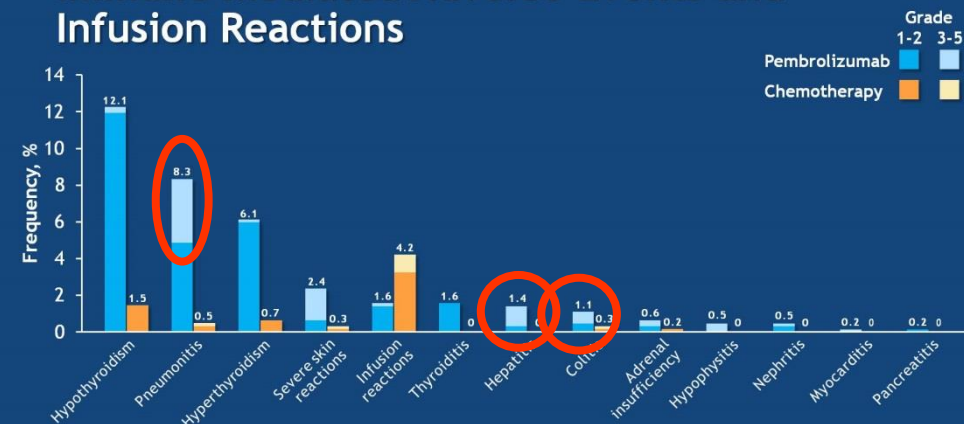
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Data cutoff date: Feb 26, 2018.

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Færre grad 3-5 bivirkninger = bedre QoL

Immune-Mediated Adverse Events and Infusion Reactions



Considered regardless of attribution to treatment or immune relatedness by the investigator. Related terms included in addition to the preferred terms listed.

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Data cutoff date: Feb 26, 2018.

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Obs IO-tox: pneumonit, hepatit, colit



Keynote-042 (Pembrolizumab) Fase 3, 1. linje til metastatisk NSCLC

Summary and Conclusions

- Pembrolizumab significantly improved OS over platinum-based chemotherapy as first-line therapy for advanced/metastatic NSCLC with PD-L1 TPS $\geq 50\%$, $\geq 20\%$, and $\geq 1\%$
 - HR (95% CI) of 0.69 (0.56-0.85), 0.77 (0.64-0.92), and 0.81 (0.71-0.93), respectively
 - Greater magnitude of benefit for pembrolizumab at higher levels of PD-L1 expression is consistent with previous studies of pembrolizumab monotherapy in metastatic NSCLC
 - In an exploratory analysis of TPS 1-49% population, HR (95% CI) was 0.92 (0.77-1.11)
- No significant PFS benefit for pembrolizumab at this analysis
 - Based on recommendation of external data monitoring committee, study is continuing to evaluate PFS based on additional follow-up
- Duration of response longer in patients treated with pembrolizumab than chemotherapy at all levels of PD-L1 expression

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Summary and Conclusions

- Despite longer exposure, frequency of treatment-related AEs was lower with pembrolizumab
 - Safety profile consistent with that previously observed for pembrolizumab
 - Better safety profile of pembrolizumab suggests it is an appropriate treatment option for any level of PD-L1 positivity
- Keynote 042 is the first study with a primary endpoint of OS to demonstrate superiority of pembrolizumab over platinum-based chemotherapy in patients with previously untreated advanced or metastatic NSCLC without EGFR mutations or ALK translocations and with a PD-L1 TPS $\geq 1\%$
- These data confirm and potentially extend the role of pembrolizumab monotherapy as a standard first-line treatment for patients with PD-L1-expressing tumors

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**Hos PD-L1 > 50%: Bedre OS + bedre QoL
= win win
Kun bedre OS ved PD-L1 > 50!**

**Keynote-042 viser bedre OS samt bedre
tox (QoL), men det er sandsynligvis PD-L1
> 50% Ptt, der løfter kurven**

NEJ009 (Gefitinib + Platin + Pemetrexed) Fase 3, 1. linje til metastatisk EGFR-mut NSCLC



Phase III Study Comparing Gefitinib Monotherapy to Combination Therapy with Gefitinib, Carboplatin, and Pemetrexed for Untreated Patients with Advanced Non-Small Cell Lung Cancer with EGFR Mutations (NEJ009)

Atsushi Nakamura¹, Akira Inoue², Satoshi Morita³, Yukio Hosomi⁴, Terufumi Kato⁵
Tatsuro Fukuhara⁶, Akihiko Gemma⁷, Kazuhisa Takahashi⁸, Yuka Fujita⁹, Toshiyuki Harada¹⁰
Koichi Minato¹¹, Kei Takamura¹², Kunihiro Kobayashi¹³, Toshihiro Nukiwa¹⁴

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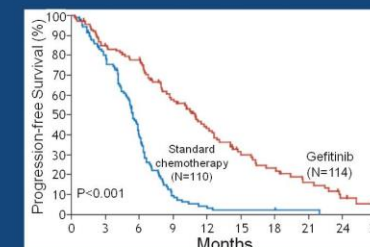
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Introduction

- EGFR-TKI alone has become a standard 1st line treatment for advanced NSCLC with EGFR sensitive mutations since pivotal studies, including our NEJ002, demonstrated its efficacy.
- In spite of significant differences in PFS between EGFR-TKI and chemotherapy, most studies have failed to show the differences in OS possibly due to a crossover use of EGFR-TKI in the control arms.
- Another concern was that only 70% of patients in the 1st line gefitinib arm received a standard post-EGFR-TKI treatment, platinum doublet, in NEJ002. Thus a thorough use of both EGFR-TKI and platinum doublet was expected to improve OS in patients with EGFR-mutated NSCLC.



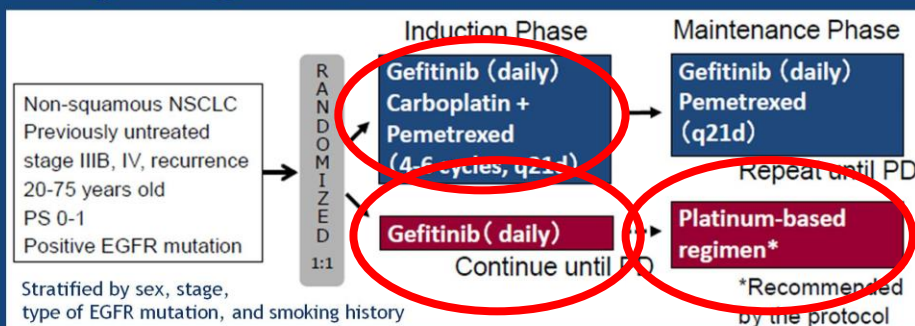
NEJ002 Maemondo, NEJM 2010

**EGFR-TKI (Gefitinib) i kombi med
KT (Platin + Pemetrexed)**

**NEJ002: 1.L mono, TT, F3
PFS ≠ OS**

NEJ009 (Gefitinib + Platin + Pemetrexed) Fase 3, 1. linje til metastatisk EGFR-mut NSCLC

Study Design of NEJ009



- From Oct. 2011 to Sep. 2014, 345 patients were enrolled from 47 institutions across Japan. In Oct. 2017, a number of pre-planned events for primary endpoint analysis were observed.

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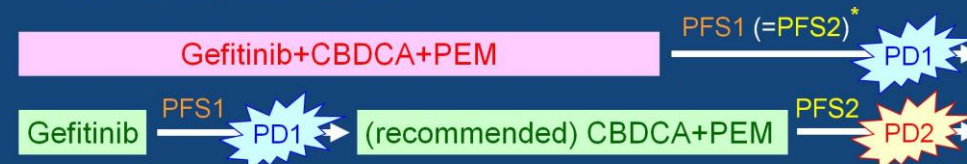
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Endpoints

- Initial protocol setting in Oct. 2011
Primary endpoint: OS
Secondary endpoints: PFS, PFS2*, ORR, Safety, QOL
- Protocol amendment in Feb. 2016 before the interim analysis
Multiple primary endpoints: PFS, PFS2*, and OS
Secondary endpoints: ORR, Safety, QOL

*PFS2 in this study indicates a comparison of PD2 in the reference arm and PD1 in the experimental arm.



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*Man bruger hurtigere begge sine våben i
kombi-behandling*

NEJ009 (Gefitinib + Platin + Pemetrexed) Fase 3, 1. linje til metastatisk EGFR-mut NSCLC

Baseline Demographics

	Gefitinib (n=172)	Gefitinib+CBDCA+PEM (n=170)
Mean age, years	64.1	64.8
Male, n (%)	64 (37.2)	56 (32.9)
Smoking history, n (%) Yes / No	75 (43.6) / 97 (56.4)	73 (42.9) / 97 (57.1)
ECOG PS, n (%) 0 / 1	107 (62.2) / 65 (37.8)	98 (57.6) / 72 (42.4)
Clinical stage, n (%) IV / post-op recurrence	138 (80.2) / 29 (16.9)	139 (81.8) / 25 (14.7)
Brain metastasis, n (%)	38 (22.1)	50 (29.6)
Adenocarcinoma, n (%)	170 (98.8)	168 (98.8)

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Exposure to Study Treatment

	Gefitinib (n=172)	Gefitinib+CBDCA+PEM (n=169)
Duration of gefitinib treatment		
Mean (SD)	462 days (373)	730 days (461)
Median (range)	348 days (29-2123)	672 days (14-1794)
CBDCA+PEM		n=168 (99.4%)
Median cycles (range)	—	4 (1-6)
PEM maintenance		n=135 (79.9%)
Median cycles (range)	—	16 (1-75)

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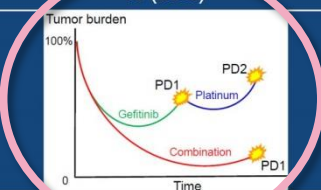
*Lidt skæv stratification (PS, Hjernemets),
men ok for løfter kontrol-Ptt*

*Kombi virker markant bedre,
pæn synergi (2 + 2 = 5)*

NEJ009 (Gefitinib + Platin + Pemetrexed) Fase 3, 1. linje til metastatisk EGFR-mut NSCLC

Clinical status at PD1 and PD2

	Gefitinib (n=172)	Gefitinib+CBDCA+PEM (n=169)
PD1	n=153	n=135
ECOG PS, n (%)		
0-1 / 2 / 3-4	134 (87.6) / 8 (5.2) / 3 (2.0)	116 (85.9) / 12 (8.9) / 4 (2.9)
Number of metastatic organs median (range)	1 (0-5)	1 (0-7)
Brain metastasis, n (%)	38 (24.8)	48 (35.6)
PD2	n=128	
ECOG PS, n (%)		
0-1 / 2 / 3-4	88 (68.8) / 19 (14.8) / 11 (8.6)	
Number of metastatic organs median (range)	2 (0-6)	
Brain metastasis, n (%)	38 (29.7)	



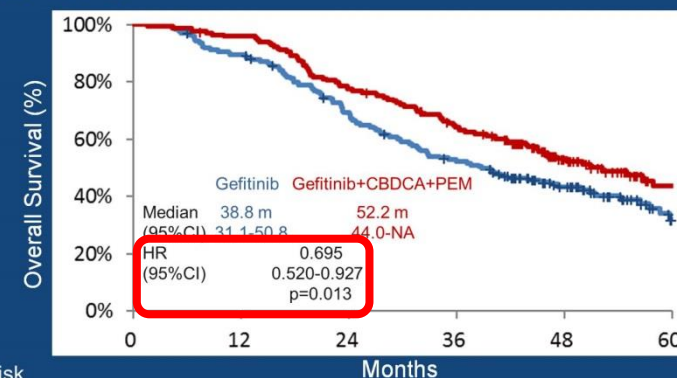
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Overall Survival



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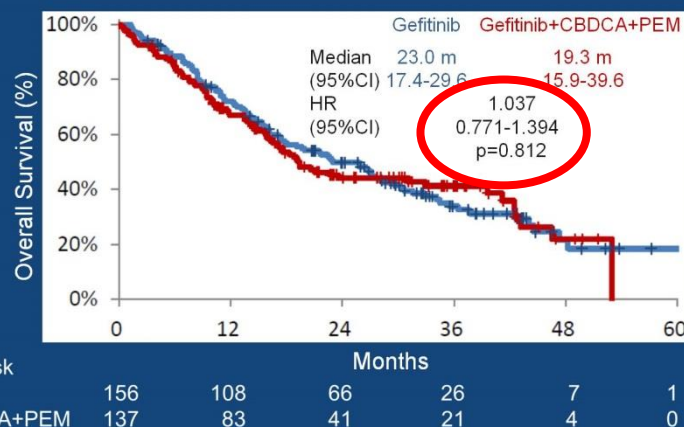
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*Kæmp det store slag up front
Træd hårdere på speederen i starten!
(Træd hurtigere på bremsen mod slutningen...)*

NEJ009 (Gefitinib + Platin + Pemetrexed) Fase 3, 1. linje til metastatisk EGFR-mut NSCLC

Survival from PD1



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Adverse Events (>20%)

	Gefitinib (n=172)		Gefitinib+CBDCA+PEM (n=169)	
	Any Grade	≥ Grade3	Any Grade	≥ Grade3
Neutropenia	7 (4.1%)	1 (0.6%)	101 (59.8%)	53 (31.4%)
Anemia	35 (20.3%)	4 (2.3%)	113 (66.9%)	36 (21.3%)
Thrombocytopenia	9 (5.2%)	0 (0%)	91 (53.8%)	29 (17.2%)
Liver Dysfunction	99 (57.6%)	37 (21.5%)	100 (59.2%)	29 (17.2%)
Creatinine Elevation	10 (5.8%)	0 (0%)	43 (25.4%)	0 (0%)
Hyponatremia	6 (3.5%)	1 (0.6%)	34 (20.1%)	5 (3%)
Diarrhea	63 (36.6%)	2 (1.2%)	60 (35.5%)	7 (4.1%)
Stomatitis	29 (16.9%)	0 (0%)	52 (30.8%)	1 (0.6%)
Rash	136 (79.1%)	5 (2.9%)	109 (64.5%)	7 (4.1%)
Nail Changes	53 (30.8%)	2 (1.2%)	41 (24.3%)	4 (2.4%)
Constipation	16 (9.3%)	0 (0%)	52 (30.8%)	0 (0%)
Anorexia	29 (16.9%)	2 (1.2%)	99 (58.6%)	12 (7.1%)
Fatigue	20 (11.6%)	0 (0%)	58 (34.3%)	6 (3.6%)

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**Ammunitionen løber tør hurtigere =
Skift fokus til QoL**

**Kombi-Tox er noget hårdere, men de
"værste" påvirker ikke direkte QoL (penier)**



NEJ009 (Gefitinib + Platin + Pemetrexed) Fase 3, 1. linje til metastatisk EGFR-mut NSCLC

Summary

- Gefitinib plus carboplatin and pemetrexed achieved superior PFS compared with gefitinib alone (HR 0.492).
- Gefitinib plus carboplatin and pemetrexed provided superior OS compared with gefitinib alone (HR 0.695), although there was no difference in PFS2 analysis.
- Clinical status at PD1 was similar between arms, and survival from PD1 was not different between arms despite the majority of patients in gefitinib alone arm receiving platinum regimen after PD1.
 - *Prolongation of PD1 is critical for EGFR-mutated patients, and PFS is a good surrogate marker for OS.*
- Hematological toxicities were more common in the combination arm although few patients discontinued due to toxicities in both arms.

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**NEJ009: OS-gevinst
og acceptabel tox (QoL)**

Baseline steroider inden Immunterapi Retrospektivt, to-center, register-studie

Deleterious Effect of Baseline Steroids on Efficacy of PD-(L)1 Blockade in Patients with Non-Small Cell Lung Cancer

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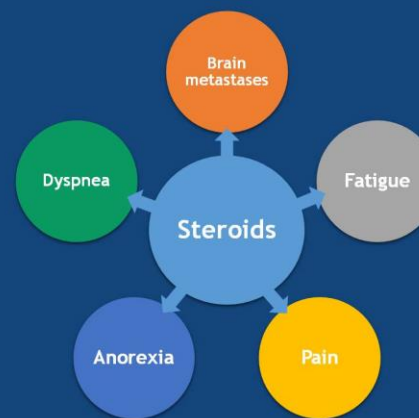
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Steroids are commonly used in cancer care



- Corticosteroids can palliate and provide rapid relief of many cancer related symptoms

- Potential toxicities of long term steroids

- Hyperglycemia
- Fluid retention
- Muscle wasting
- Immunosuppression

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**Wonder-drug hos KT-Ptt,
men hvad med IO-Ptt?**

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Steroids and PD-(L)1 Blockade

- Steroids are the mainstay of treatment for immune related adverse events (irAEs)
 - Use of steroids to treat irAEs does not appear to diminish efficacy of PD-(L)1 blockade

Efficacy in patients receiving baseline steroids is unknown

- Patients on baseline steroids (prednisone ≥ 10 mg) were not eligible for clinical trials of PD-(L)1 inhibitors
- Mechanism of action of PD-(L)1 blockade may include “proliferative burst” of CD8+ T-cells

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Methods

Memorial Sloan
Kettering Cancer
Center
(n=455)

Gustave Roussy
Cancer Center
(n=185)

- Retrospective Review
- Patients with advanced NSCLC treated with single-agent PD-(L)1 inhibitor
- Medical records reviewed to identify steroid use on Day 1 of treatment (≥ 10 mg prednisone)

- ORR by RECIST
- PFS
- OS from start of treatment

Cohorts analyzed independently

- ORR by RECIST
- PFS
- OS from start of treatment

Pooled subgroup and multivariate analysis

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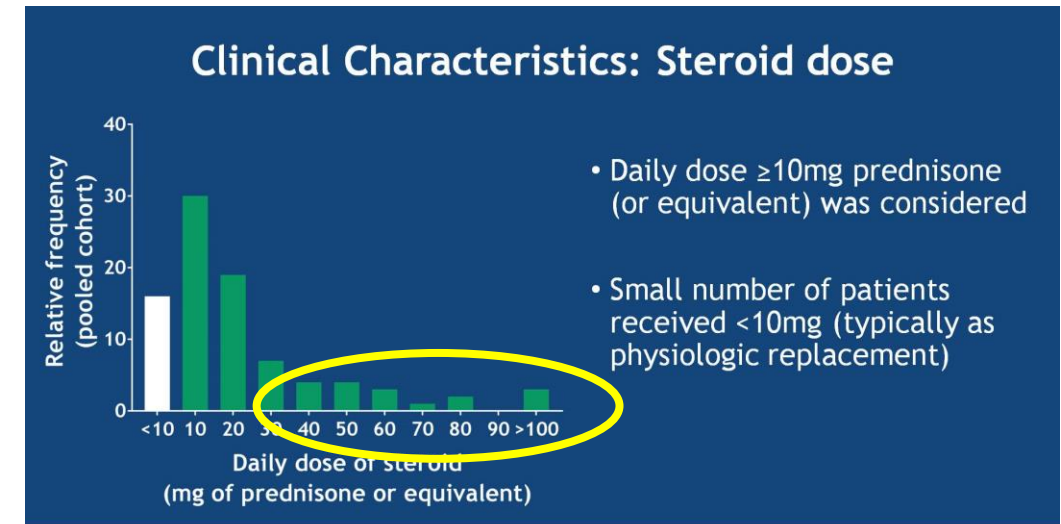


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*Er steroid-forbrug en prediktor for OS?
- er alle IO-studierne så biased?*

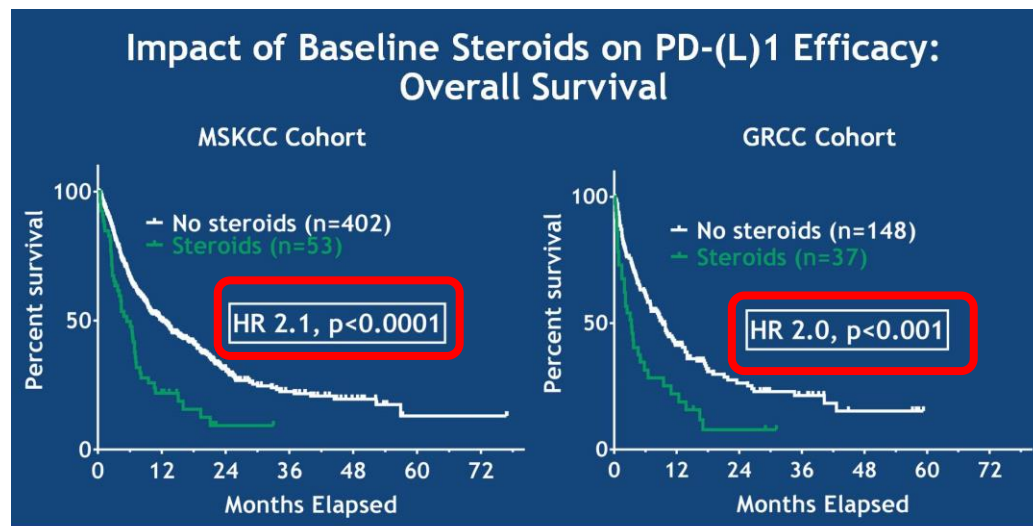
Baseline steroider inden immunterapi Retrospektivt, to-center, register-studie

Patient Characteristics	MSKCC % (n=455)	GRCC % (n=185)
Median age (range)	66 (31-93)	61 (29-84)
Men	48 (220)	66 (122)
Performance status		
ECOG 0	19 (86)	12 (22)
ECOG 1	70 (320)	66 (122)
ECOG ≥ 2	11 (49)	22 (41)
Smoking status		
Former/current	83 (376)	87 (161)
Never	17 (79)	10 (19)
Histology		
Adenocarcinoma	76 (347)	73 (116)
Squamous	18 (80)	26 (49)
NSCLC-Other	6 (28)	11 (20)
Indication for steroid use ≥ 10 mg	12% (n = 53)	20% (n = 37)
Dyspnea	30 (15)	41 (15)
Fatigue	33 (18)	3 (1)
Brain metastases	13 (7)	27 (10)
Pain	9 (5)	11 (6)
Other	15 (8)	14 (5)



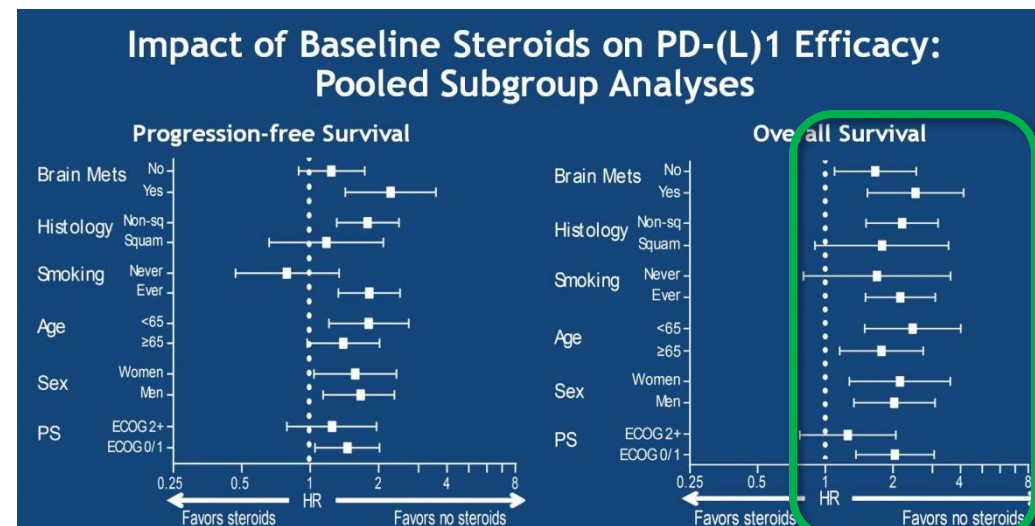
Er steroider ved baseline en driver for dårlig OS, eller blot en "passenger" markør?

Baseline steroider inden immunterapi Retrospektivt, to-center, register-studie



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Nedsætter baseline steroider IO-effekten, eller er det blot en prædikator?

Signalet er tydeligt, men årsagen uklar

Baseline steroider inden immunterapi Retrospektivt, to-center, register-studie

Impact of Baseline Steroids on PD-(L)1 Efficacy: Multivariate Analysis

Patient characteristics	ORR Odds Ratio (95% CI)	p-value	PFS Hazard Ratio (95% CI)	p-value	OS Hazard Ratio (95% CI)	p-value
Smoking status (never vs ever)	0.33 (0.15-0.74)	0.007	1.64 (1.30-2.04)	<0.001	1.03 (0.81-1.33)	0.78
Performance status (ECOG ≥2 vs 0/1)	0.29 (0.11-0.75)	0.11	1.97 (1.55-2.50)	<0.001	2.29 (1.75-2.98)	<0.001
History of brain metastases (yes vs no)	0.88 (0.52-1.49)	0.6	1.16 (0.96-1.41)	0.1	1.37 (1.11-1.7)	0.003
Steroid use (yes vs no)	0.42 (0.17-1.01)	0.053	1.31 (1.03-1.67)	0.03	1.66 (1.28-2.16)	<0.001

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Baseline steroids and PD-(L)1 Efficacy: Conclusions

- Baseline steroid use when starting PD-(L)1 blockade is associated with inferior outcomes (PFS and OS)
 - Effect may be predictive and/or prognostic
- Prudent use of steroids in patients for whom PD-(L)1 blockade is planned should be considered
 - Consideration of non-steroid alternatives for management of cancer symptoms
 - Medically necessary steroids (e.g. brain metastases) should NOT be avoided
- Implications for patients receiving chemo + PD-(L)1 is uncertain

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Øget opmærksomhed på pn steroid ved IO-start.

Altid steroid ved hjernemetastaser!

Hvad er fremtidens højdespringere?

IO kombineret med RT

- A 8510** F2, NSCLC, stadie III (NICOLAS)
1L: IO (Nivolumab) + KT (Platin/dublet) + RT
- A 9023** F2, NSCLC, stage IV (PEMBRO-RT)
1L: IO (Pembrolizumab) + SBRT
- PACIFIC** F3, NSCLC, stadie III
Adj: IO (Durvalumab) + RT



Neo-adj IO/TKI (+KT) før OP

- A 8521** F2 NSCLC, stage IIIa (NADIM-SLCG)
Neoadj: IO (Nivolumab) + KT (Platin/Paclitaxel)
- A 8532** F2, NSCLC, stage Ib – IIIa
Neoadj: IO (Atezolizumab) + KT (Platin/Paclitaxel)
- A 8541** F2, NSCLC, stage Ib-IIIb (LCMC3)
Neoadj: IO (Atezolizumab) mono
- A 8544** F2, NSCLC, EGFR+, stage III (ASCENT)
Neoadj: TT (Afatinib) + KT(Platin/Pemetrexed) + RT

Hvem er fremtidens højdespringere? Hvilke Fase 2/3 studier kommer over baren?

KT + IO kombi

A 105 F3, NSCLC, stage IV (Keynote-407)
1L: IO (Pembrolizumab) + KT (Platin/Taxan)

A 9001 F3, NSCLC, stage IV, PDL1 <1 (Checkmate 227)
1L: IO (Nivolumab) + KT (Platin/Dublet)

A 9026 F2, NSCLC, stage IIIb/IV (Keynote-021)
1L: IO (Pembrolizumab) + KT (Platin/Pemetrexed)

LBA 9000 F3, NSCLC, stage IV (IMPOWER 131)
1L: IO (Atezolizumab) + KT (Platin/Taxan)

SCLC

A 8575 F2, SCLC, ED
2L: IO (Pembrolizumab) + KT (Paclitaxel)





Hvad bringer fremtiden?

Nu og nær fremtid

- ✓ PD-L1 >50%: 1.L IO (Pembrolizumab) (KN-024)
- ✓ PD-L1 1-49%: 1.L IO + KT kombi (KN-189)
- ✓ Adjuverende IO efter konkomitant KT + RT (PACIFIC)

Inden for de næste 5 år

- ✓ Implementering af TMB, IO-dublet (PD-(L)1 + CTLA-4) til TMB high
- ✓ Neoadjuverende IO før OP
- ✓ Konkomitant IO + KT + RT
- ✓ Kombinationbehandling til st. IV IO + KT + RT



Hvad bringer fremtiden?

Uafklarede spørgsmål

- ✓ Hvordan behandles PD-L1 <1% bedst?
- ✓ Hvilken kemo "backbone" er bedst i kombi med IO?
- ✓ Korrekt rækkefølge af KT, RT, IO, TT og OP?
- ✓ Steroider samtidigt med IO?
- ✓ Hvad med SCLC?



Tak

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Peter Michael Vestlev

Overlæge
Lægelig leder i SKA



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Herlev Hospital, Onkologisk Afd.
Lunge Team





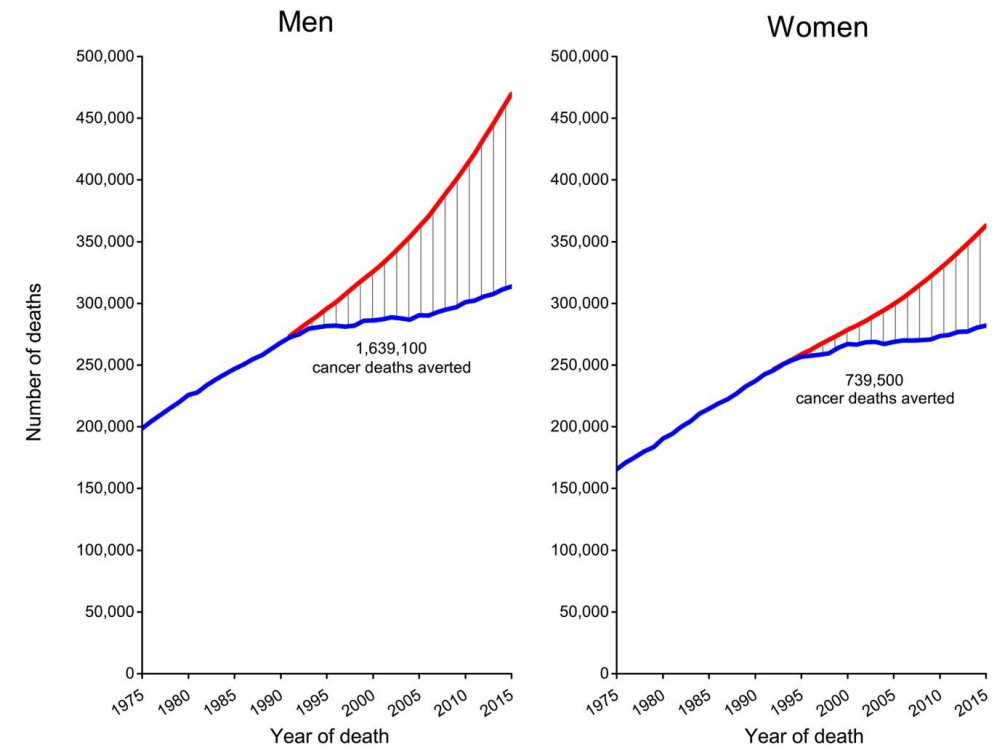
Tak

SKA - Sammenslutningen af KræftAfdelinger



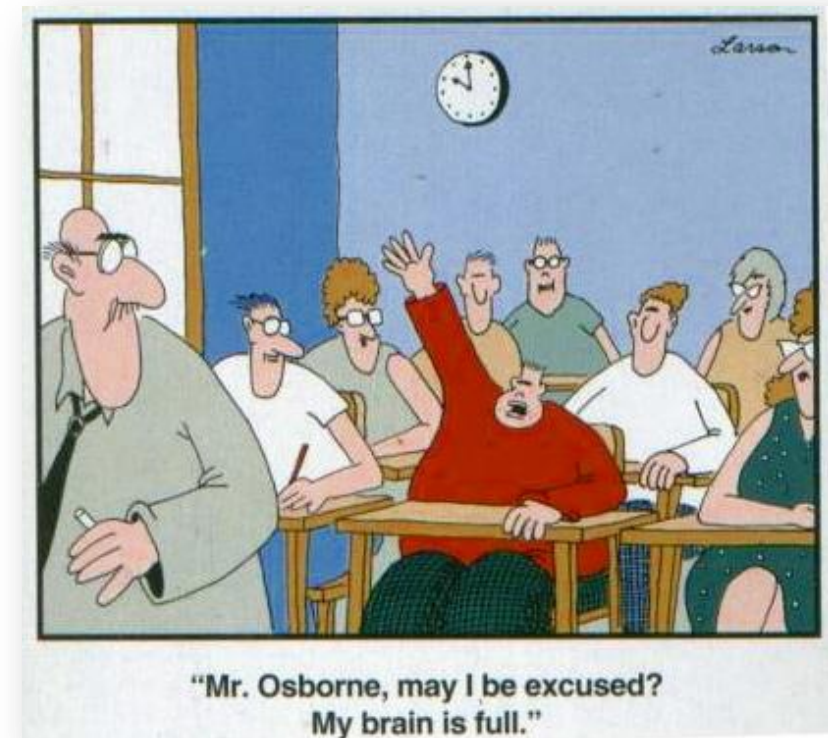
abbvie

SAVE SKA og post-ASCO 2019



**Antal undgåede cancer –relaterede dødfald
USA, 1991-2015**

Spørgsmål?





Post-ASCO

Lungekræft

Gitte Fredberg Persson, overlæge ph.d.

Jakob Johansen, klinisk assistent

Kræftafdelingen på Herlev Hospital



Stadie	Behandling	Overlevelse (5 år)	Nye behandlinger på vej
I	Kirurgi stereotaktisk stråleterapi	77-92%*	
II	Kirurgi + forebyggende kemoterapi	53-60%*	Neoadj immunterapi (adj?)
III	Stråleterapi + kemoterapi	13-36%*	Immunterapi + KT+RT
IV	Immunoterapi Kemoterapi Målrettet terapi Strålebehandling	0-10%*	IO baseret kombinationsbehandling
*Detterbeck et al. J Thor Oncol, 11 (9) (2016), pp. 1433-1446			



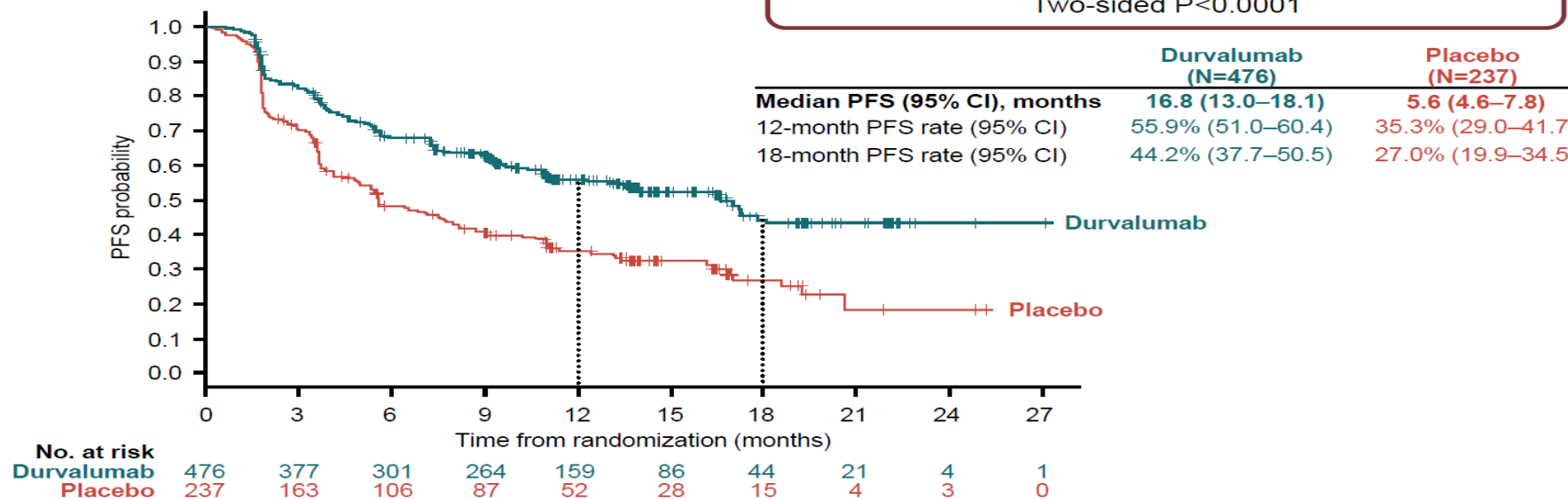
PACIFIC

adj. Durvalumab efter KRT til LA-NSCLC

MADRID 2017 **ESMO** congress

PFS by BICR (Primary Endpoint; ITT)

Stratified hazard ratio, 0.52 (95% CI, 0.42–0.65)
 Two-sided P<0.0001

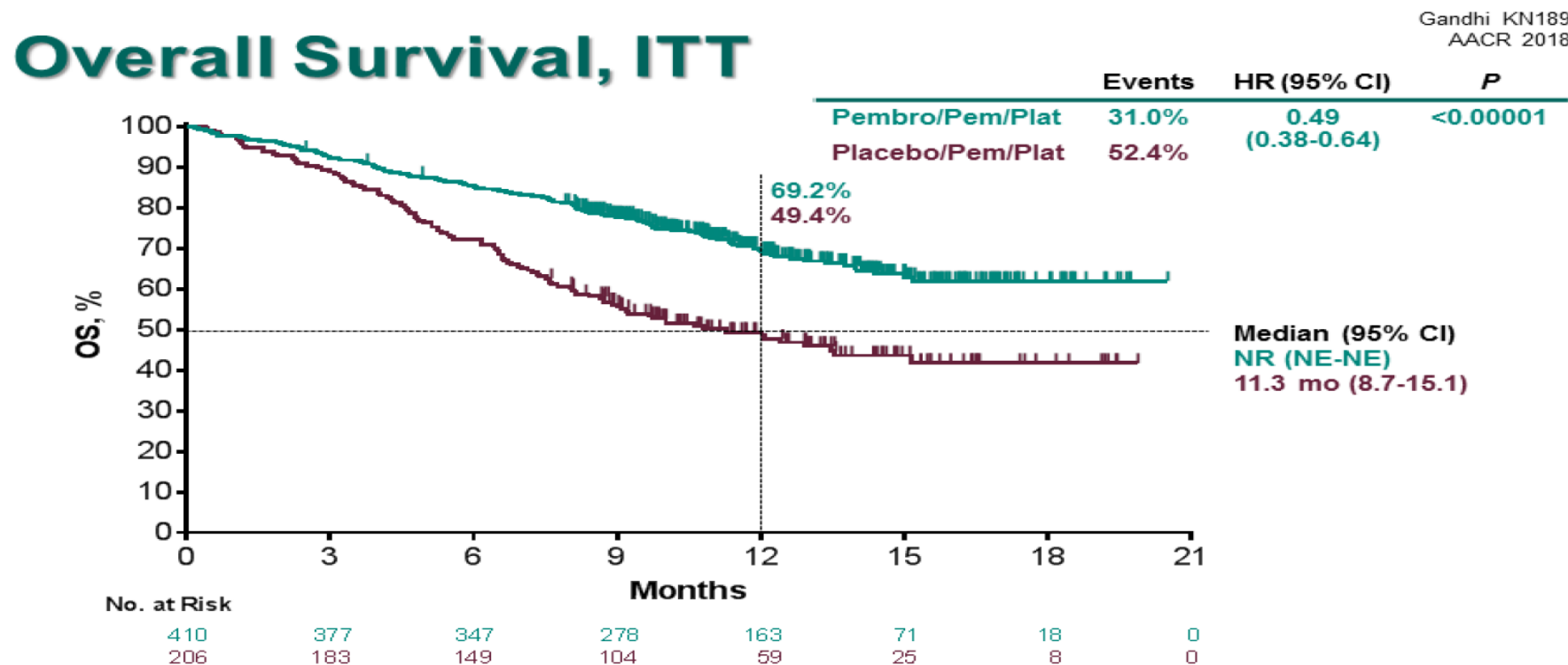


BICR, blinded independent central review; CI, confidence interval; ITT, intention-to-treat; PFS, progression-free survival



Keynote 189

Kemo- og immunterapi til stadie IV NSCLC



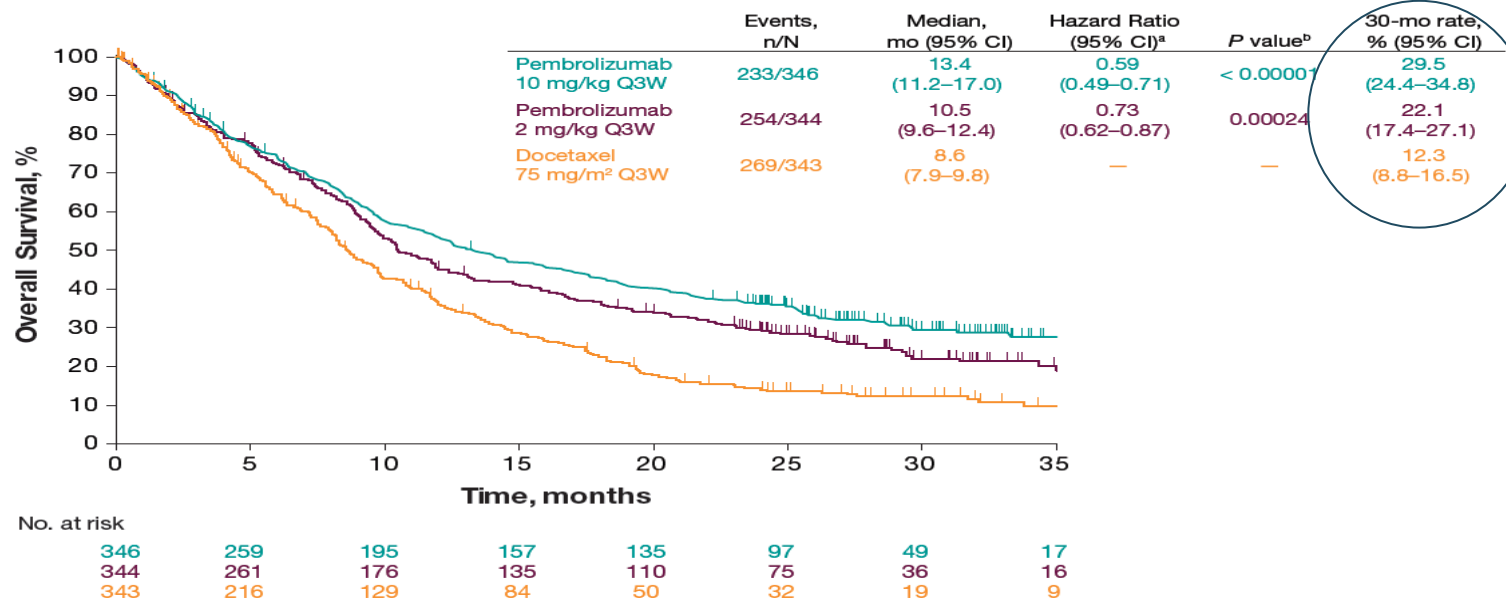


Keynote001

Fordoblet langtidsoverlevelse (3 år)

Overall Survival

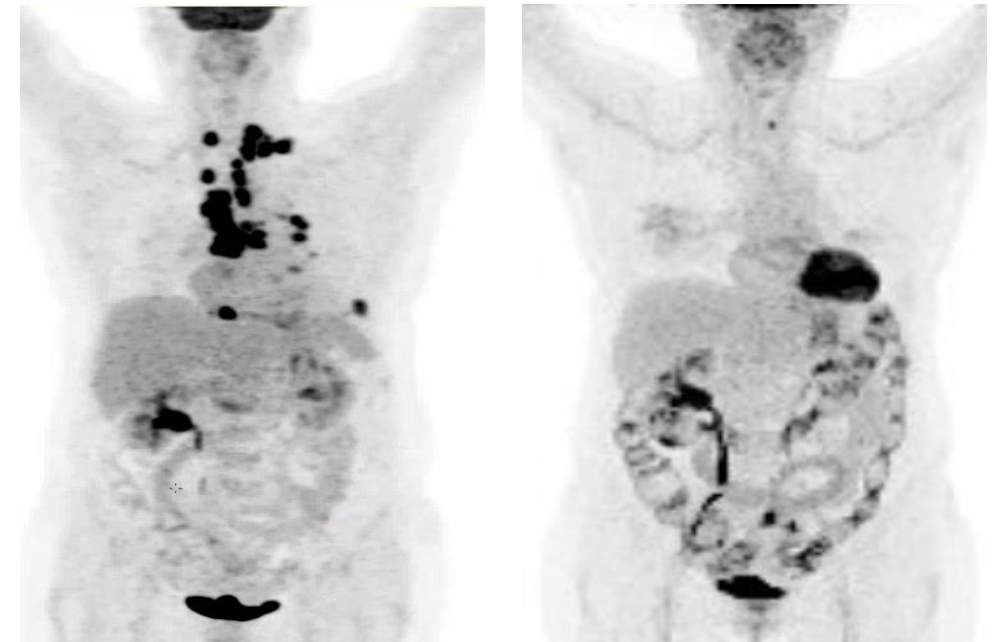
Figure 2. Kaplan-Meier Estimates of OS



Case

Fantastisk effekt

- 67 årig kvinde med adenokarcinom i venstre lunge
- Jan 2017, helhjernebestråling og 4 serier kemoterapi → stabile forhold
- Maj 2017, progression. Starter PD-1 hæmmer
- Nov 17, resterer kun svulst i venstre lunge, strålebehandles
- Feb 2018, ingen tegn til restsygdom (fraset synkron c. thyroidea)

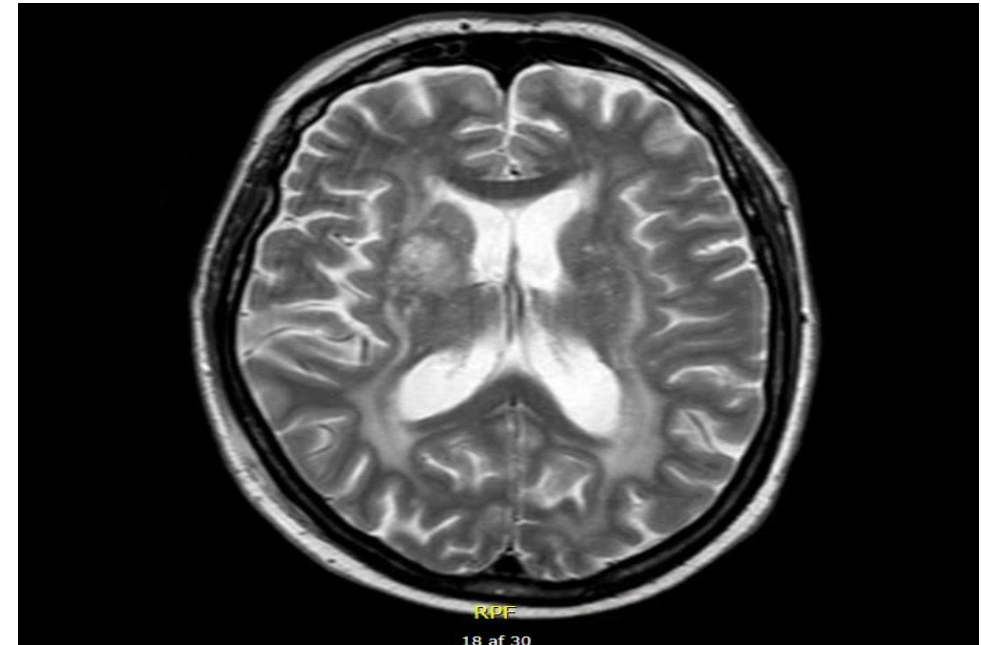




Patient historie

Alvorlige bivirkninger

- Marts 18, indlægges efter krampeanfald. MR af hjernen viser subakut infarkt og strålefølger.
- April 18, udskrives til genoptræning. Tilstanden forværres, tilskrives senfølger efter stråleterapi og blodpropper.
- Overflyttes til hospice af familien
- Maj 18, starter behandling med binyrebarkhormon på mistanke om immunudløst hjernebetændelse
- Betydelig bedring





Konklusion

- De fleste patienter med NSCLC i god PS skal have PD-(L)1 hæmmer i fremtiden
- Neoadjuvant, adjuvant, konkomitant, 1. linje
- Kombination med CTLA-4 hæmmere, KT, RT, operation,