COMBINING IMMUNOTHERAPY WITH RADIATION IN THORACIC MALIGNANCIES

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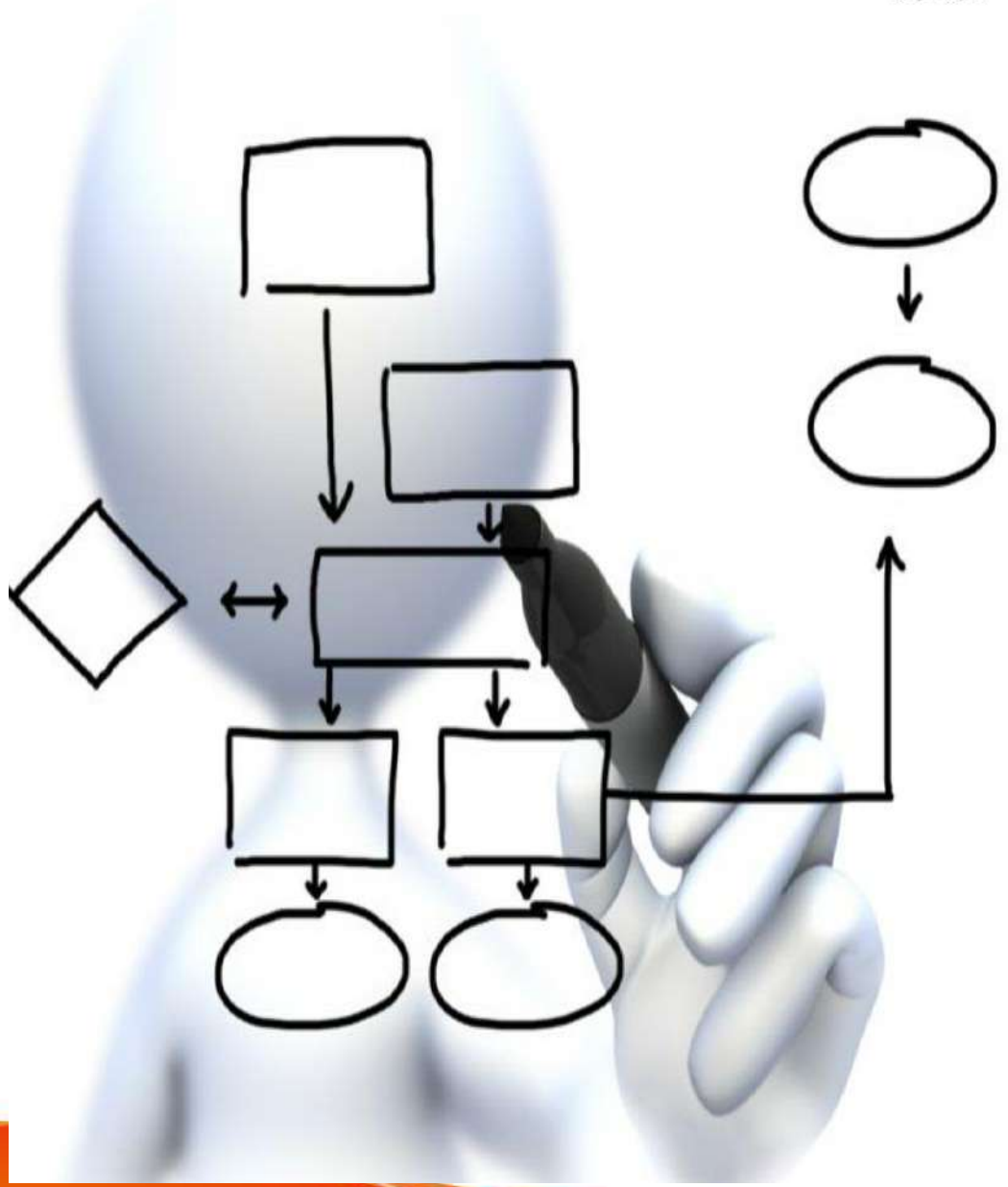
RADIATION ONCOLOGY

HCG, BANGALORE

Flow...

- Role of immunotherapy
- ImmunoRT- rationale
- Current evidence
- when where and how
- our experience
- future directions



Immunotherapy in NSCLC

TRIAL	YEAR	DRUG	STAGE	PDL 1 INCLUSION	CONTROL ARM	RESULTS
CHECKMATE017	phase III 2015	NIVOLUMAB	IIIB/IV A SQUAMOUS NSCLC	NA	Vs Docetaxel	OS ↑↑ RR ↑↑ PFS ↑↑
CHECKMATE057	phase III 2015	NIVOLUMAB	IIIB/IV A NON SQUAMOUS NSCLC	NA	Vs Docetaxel	OS ↑↑ RR ↑↑ PFS ↑↑
KEYNOTE0	PHASE III	PEMBROLIZ	IV(failed on	> 1%	Vs Docetaxel	OS

The NEW ENGLAND JOURNAL of MEDICINE

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Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

METHODS

We randomly assigned patients, in a 2:1 ratio, to receive durvalumab (at a dose of 10 mg per kilogram of body weight intravenously) or placebo every 2 weeks for up to 12 months. The study drug was administered 1 to 42 days after the patients had received chemoradiotherapy. The coprimary end points were progression-free survival (as assessed by means of blinded independent central review) and overall survival (unplanned for the interim analysis). Secondary end points included 12-month and 18-month progression-free survival rates, the objective response rate, the duration of response, the time to death or distant metastasis, and safety.

RESULTS

Of 713 patients who underwent randomization, 709 received consolidation therapy (473 received durvalumab and 236 received placebo). The median progression-free survival from randomization was 16.8 months (95% confidence interval [CI], 13.0 to 18.1) with durvalumab versus 5.6 months (95% CI, 4.6 to 7.8) with placebo (stratified hazard ratio for disease progression or death, 0.52; 95% CI, 0.42 to 0.65; P<0.001); the 12-month progression-free survival rate was 55.9% versus 35.3%, and the 18-month progression-free survival rate was 44.2% versus 27.0%. The response rate was higher with durvalumab than with placebo (28.4% vs. 16.0%; P<0.001), and the median duration of response was longer (72.8% vs. 46.8% of the patients had an ongoing response at 18 months). The median time to death or distant metastasis was longer with durvalumab than with placebo (23.2 months vs. 14.6 months; P<0.001). Grade 3 or 4 adverse events occurred in 29.9% of the patients who received durvalumab and 26.1% of those who received placebo; the most common adverse event of grade 3 or 4 was pneumonia (4.4% and 3.8%, respectively). A total of 15.4% of patients in the durvalumab group and 9.8% of those in the placebo group discontinued the study drug because of adverse events.

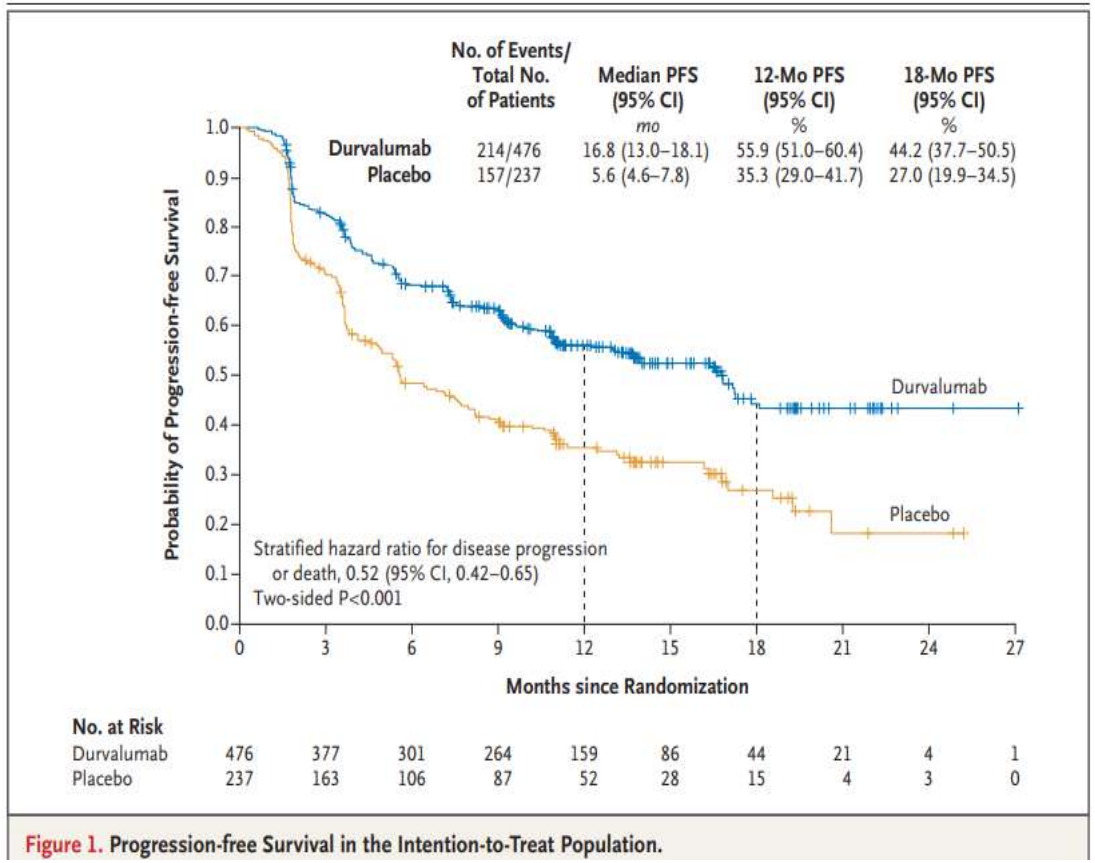
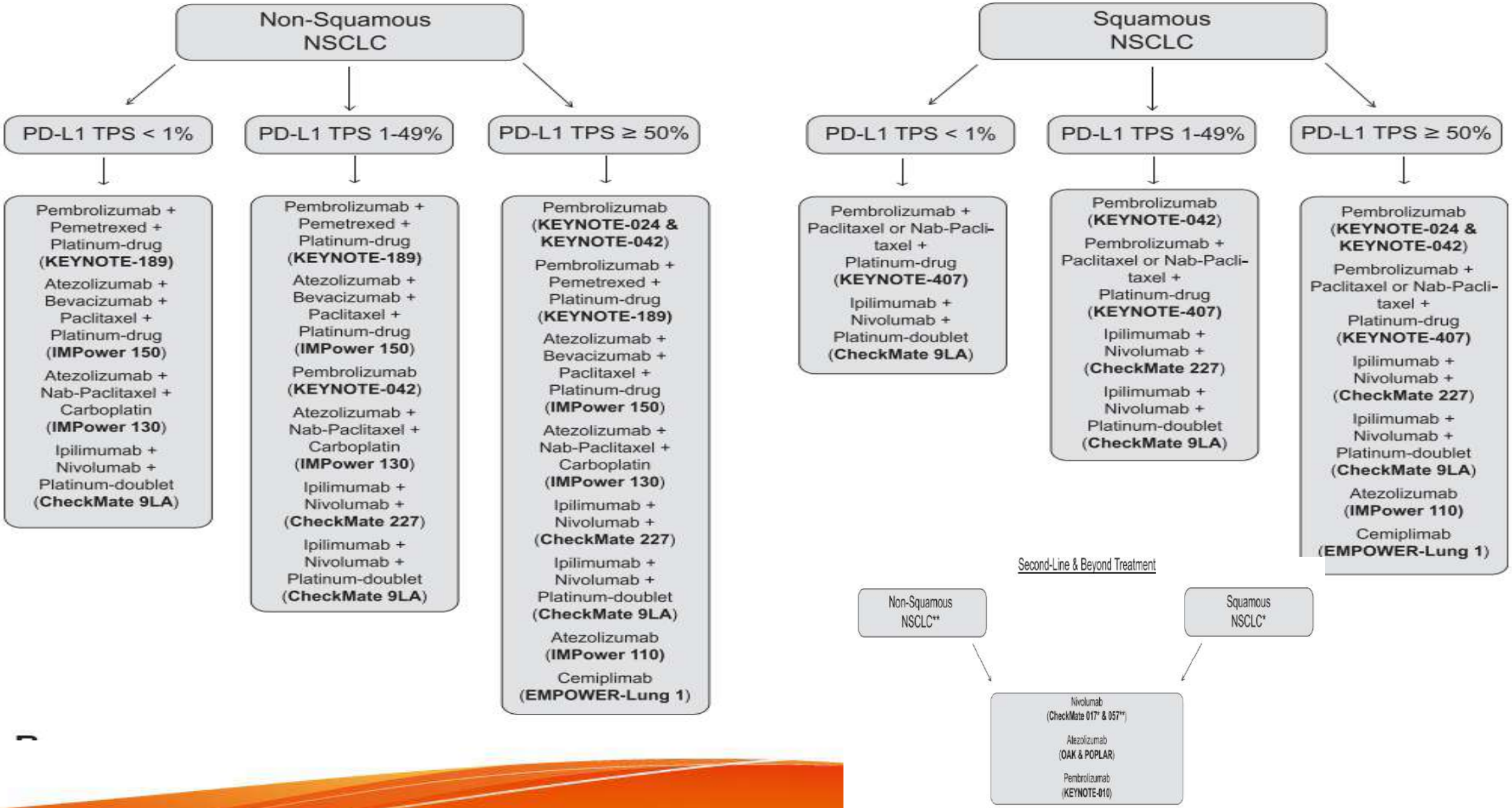
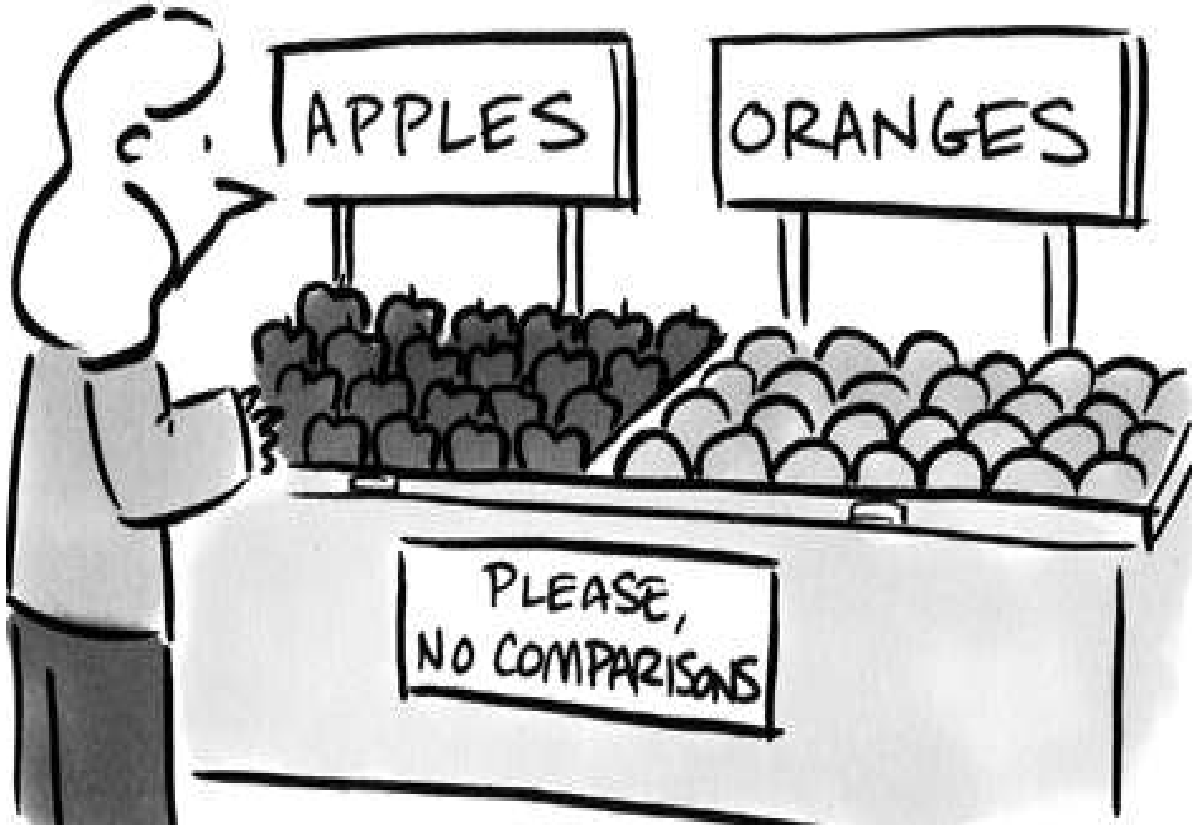


Figure 1. Progression-free Survival in the Intention-to-Treat Population.


Non-Squamous NSCLC
PD-L1 TPS < 1%
Pembrolizumab + Pemetrexed + Platinum-drug (KEYNOTE-189)
Atezolizumab + Bevacizumab + Paclitaxel + Platinum-drug (IMPower 150)
Atezolizumab + Nab-Paclitaxel + Carboplatin (IMPower 130)
Ipilimumab + Nivolumab + Platinum-doublet (CheckMate 9LA)
PD-L1 TPS 1-49%
Pembrolizumab + Pemetrexed + Platinum-drug (KEYNOTE-189)
Atezolizumab + Bevacizumab + Paclitaxel + Platinum-drug (IMPower 150)
Pembrolizumab (KEYNOTE-042)
Atezolizumab + Nab-Paclitaxel + Carboplatin (IMPower 130)
Ipilimumab + Nivolumab + (CheckMate 227)
Ipilimumab + Nivolumab + Platinum-doublet (CheckMate 9LA)
PD-L1 TPS ≥ 50%
Pembrolizumab (KEYNOTE-024 & KEYNOTE-042)
Pembrolizumab + Pemetrexed + Platinum-drug (KEYNOTE-189)
Atezolizumab + Bevacizumab + Paclitaxel + Platinum-drug (IMPower 150)
Atezolizumab + Nab-Paclitaxel + Carboplatin (IMPower 130)
Ipilimumab + Nivolumab + (CheckMate 227)
Ipilimumab + Nivolumab + Platinum-doublet (CheckMate 9LA)
Atezolizumab (IMPower 110)
Cemiplimab (EMPOWER-Lung 1)
Squamous NSCLC
PD-L1 TPS < 1%
Pembrolizumab + Paclitaxel or Nab-Paclitaxel + Platinum-drug (KEYNOTE-407)
Ipilimumab + Nivolumab + Platinum-doublet (CheckMate 9LA)
PD-L1 TPS 1-49%
Pembrolizumab (KEYNOTE-042)
Pembrolizumab + Paclitaxel or Nab-Paclitaxel + Platinum-drug (KEYNOTE-407)
Ipilimumab + Nivolumab + (CheckMate 227)
Ipilimumab + Nivolumab + Platinum-doublet (CheckMate 9LA)
PD-L1 TPS ≥ 50%
Pembrolizumab (KEYNOTE-024 & KEYNOTE-042)
Pembrolizumab + Paclitaxel or Nab-Paclitaxel + Platinum-drug (KEYNOTE-407)
Ipilimumab + Nivolumab + (CheckMate 227)
Ipilimumab + Nivolumab + Platinum-doublet (CheckMate 9LA)
Atezolizumab (IMPower 110)
Cemiplimab (EMPOWER-Lung 1)
Second-Line & Beyond Treatment
Non-Squamous NSCLC**
Squamous NSCLC*
Nivolumab (CheckMate 017* & 057**)
Atezolizumab (OAK & POPLAR)
Pembrolizumab (KEYNOTE-010)


APPLES
ORANGES
PLEASE,
NO COMPARISONS

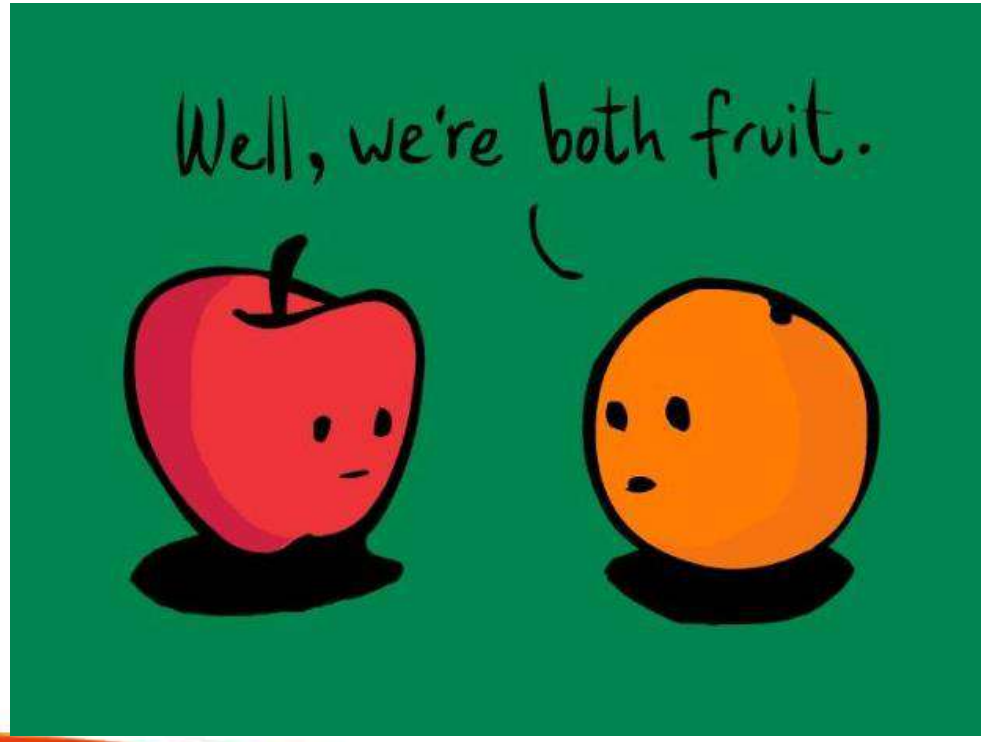
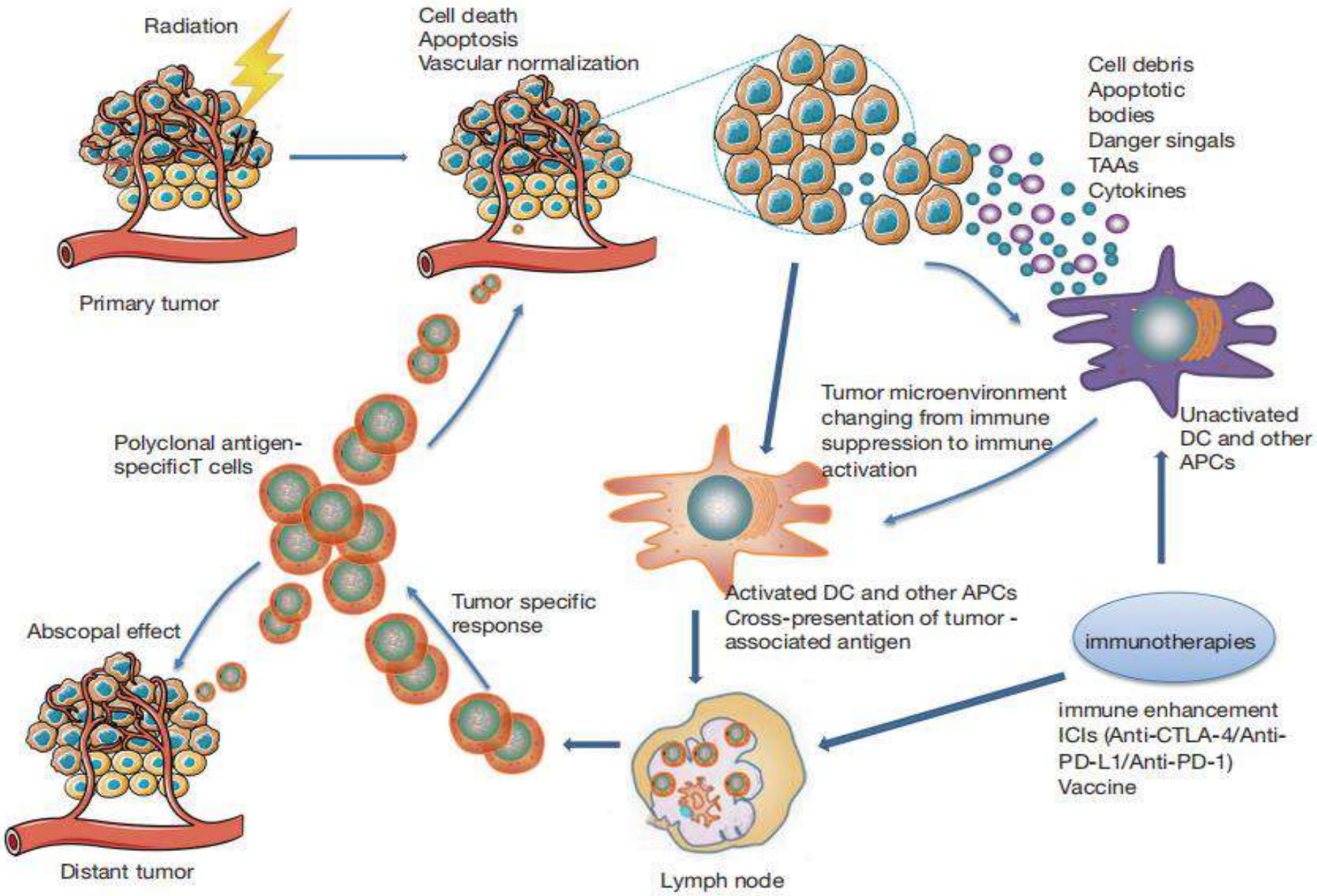

Well, we're both fruit.

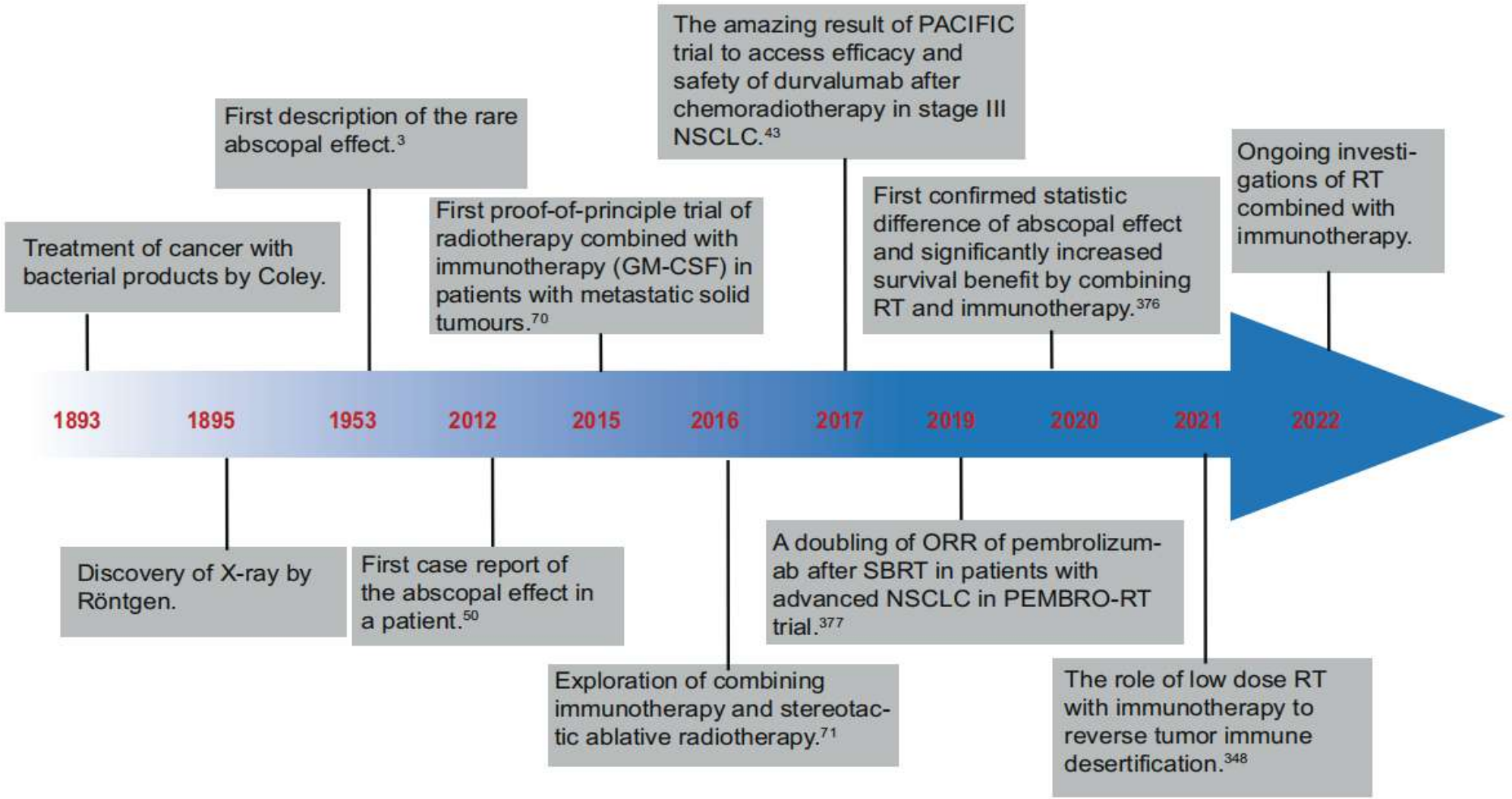
Table 3. Key studies in first-line NSCLC

Phase III study	Population	Treatment groups	HR, overall survival (m)
KEYNOTE-024	Untreated advanced NSCLC (no EGFR or ALK mutation) PD-L1 TPS _50%	Pembrolizumab versus Platinum-based chemotherapy	HR, 0.63 mOS, 30.0 months versus 14.2 months
KEYNOTE-042	Untreated locally advanced or metastatic NSCLC PD-L1 TPS_1%	Pembrolizumab versus Platinum-based chemotherapy	HR, 0.81 mOS, 16.7 months versus 12.1 months
KEYNOTE-189	Metastatic nonsquamous NSCLC (no EGFR or ALK mutation	Carboplatin/cisplatin pemetrexed pembrolizumab Carboplatin/cisplatin pemetrexed	HR, 0.49, 12-m OS, 69.2% versus 49.4%
KEYNOTE-407	Metastatic squamous NSCLC	Carboplatin/paclitaxel or nab-paclitaxel pembrolizumab Carboplatin/paclitaxel or nab-paclitaxel	HR, 0.64 mOS, 15.9 months versus 11.3 months
Checkmate 026	Stage IV or recurrent NSCLC PD-L1_1%	Nivolumab Platinum-based Chemotherapy	HR, 1.02 mOS, 14.4 months versus 13.2 months
Checkmate 227	Stage IV or recurrent NSCLC PD-L1 _1%	Nivolumab-ipilimumab versus Platinum-based chemotherapy	HR, 0.79 mOS, 17.1 months versus 14.9 months
IMpower 150	Metastatic nonsquamous NSCLC	Atezolizumab carboplatin/paclitaxel bevacizumab versus carboplatin/paclitaxel bevacizumab	HR, 0.78 mOS, 19.2 months versus 14.7 months
IMpower 110	Metastatic NSCLC (TC≥50% or IC≥10% stratified subgroup)	Atezolizumab versus cis/carboplatin pemetrexed (nonsquamous) or cis/carboplatin gemcitabine (squamous)	HR, 0,59 mOS 20.2 months versus 13.1 months

IMMUNORADIOTHERAPY


Radiation
Cell death
Apoptosis
Vascular normalization
Cell debris
Apoptotic
bodies
Danger singals
TAAs
Cytokines
Primary tumor
Tumor microenvironment
changing from immune
suppression to immune
activation
Unactivated
DC and other
APCs
Polyclonal antigen-
specificT cells
Activated DC and other APCs
Cross-presentation of tumor -
associated antigen
immunotherapies
Tumor specific
response
Abscopal effect
immune enhancement
ICIs (Anti-CTLA-4/Anti-
PD-L1/Anti-PD-1)
Vaccine
Distant tumor
Lymph node

I ♥ HISTORY



Radiotherapy combined with immunotherapy: the dawn of cancer treatment

JAMA Oncology | Original Investigation

Effect of Pembrolizumab After Stereotactic Body Radiotherapy vs Pembrolizumab Alone on Tumor Response in Patients With Advanced Non–Small Cell Lung Cancer

Results of the PEMBRO-RT Phase 2 Randomized Clinical Trial

INTERVENTIONS Pembrolizumab (200 mg/kg every 3 weeks) either alone (control arm) or after radiotherapy (3 doses of 8 Gy) (experimental arm) to a single tumor site until confirmed radiographic progression, unacceptable toxic effects, investigator decision, patient withdrawal of consent, or a maximum of 24 months.

MAIN OUTCOMES AND MEASURES Improvement in overall response rate (ORR) at 12 weeks from 20% in the control arm to 50% in the experimental arm with $P < .10$.

RESULTS Of the 92 patients enrolled, 76 were randomized to the control arm (n = 40) or the experimental arm (n = 36). Of those, the median age was 62 years (range, 35-78 years), and 44 (58%) were men. The ORR at 12 weeks was 18% in the control arm vs 36% in the experimental arm ($P = .07$). Median progression-free survival was 1.9 months (95% CI, 1.7-6.9 months) vs 6.6 months (95% CI, 4.0-14.6 months) (hazard ratio, 0.71; 95% CI, 0.42-1.18; $P = .19$), and median overall survival was 7.6 months (95% CI, 6.0-13.9 months) vs 15.9 months (95% CI, 7.1 months to not reached) (hazard ratio, 0.66; 95% CI, 0.37-1.18; $P = .16$). Subgroup analyses showed the largest benefit from the addition of radiotherapy in patients with PD-L1–negative tumors. No increase in treatment-related toxic effects was observed in the experimental arm.

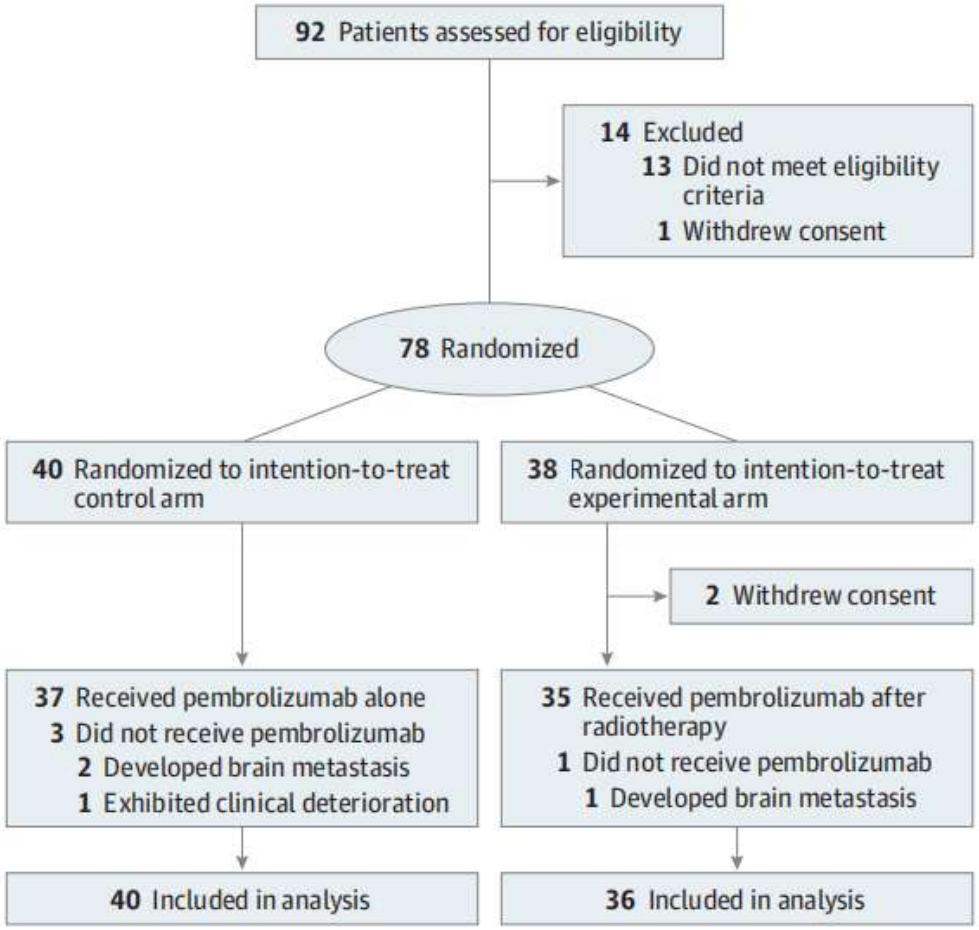
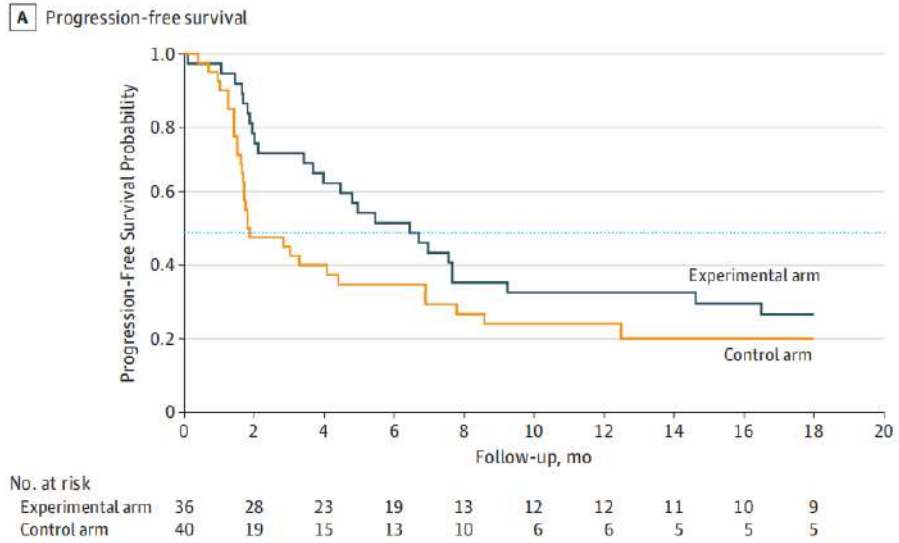
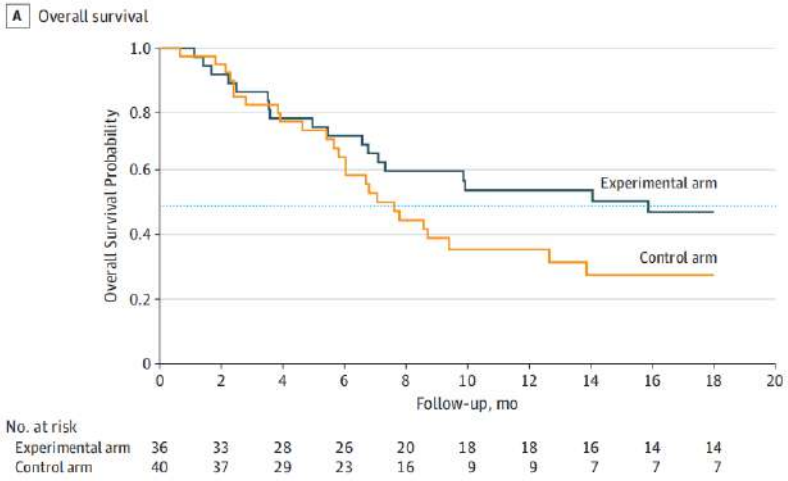


Table. Response to Treatment

Response	Experimental Arm, No./Total No. (%) (n = 36)[a]	Control Arm, No./Total No. (%) (n = 40)[b]
Best overall response, No.		
Complete response	3	1
Partial response	14	8
Stable disease	9	10
Progressive disease	10	21
Objective response rate at 12 wk		
Overall[c]	13/36 (36)	7/40 (18)
PD-L1 TPS, %		
0	4/18 (22)	1/25 (4)
1-49	3/8 (38)	3/8 (38)
≥50	6/10 (60)	3/5 (60)
Disease control rate at 12 wk[d]	23/36 (64)	16/40 (40)





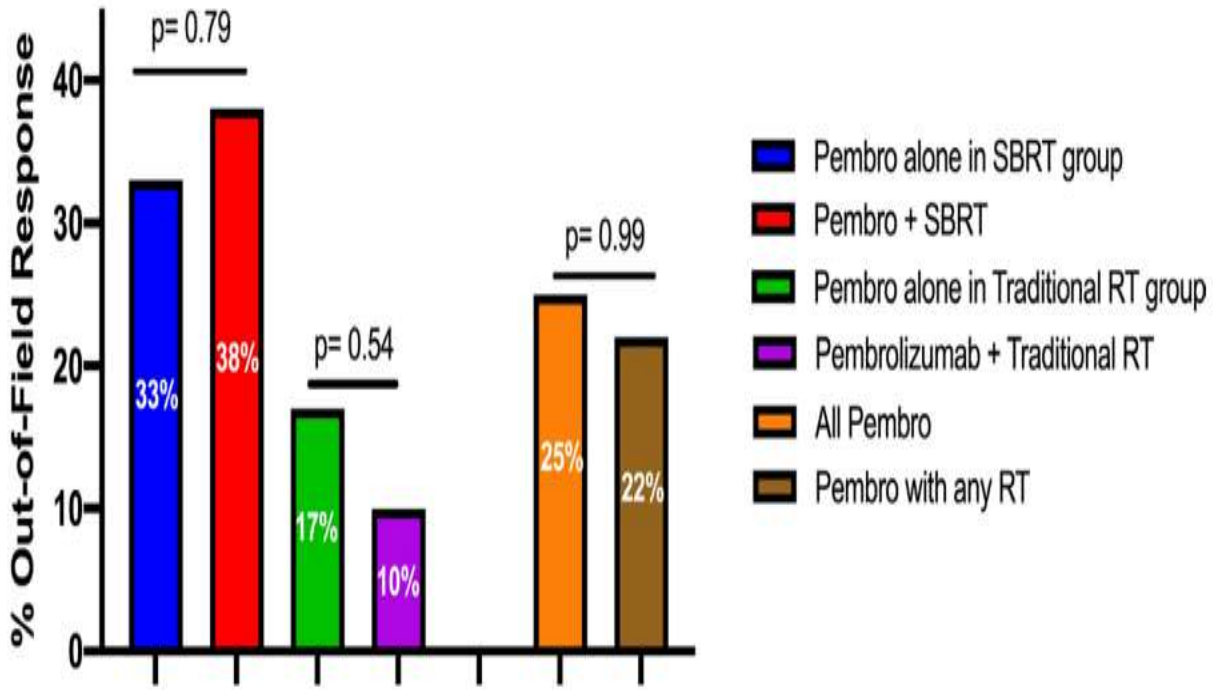
Journal for ImmunoTherapy of Cancer

Pembrolizumab with or without radiation therapy for metastatic non-small cell lung cancer: a randomized phase I/II trial

Background In this phase I/II trial, we evaluated the safety and effectiveness of pembrolizumab, with or without concurrent radiotherapy (RT), for lung and liver lesions from metastatic non-small cell lung cancer (mNSCLC).

Methods Patients with lung or liver lesions amenable to RT plus at least one additional non-contiguous lesion were included regardless of programmed death-ligand 1 (PD-L1) status. Pembrolizumab was given at 200 mg every 3 weeks for up to 32 cycles with or without concurrent RT. Metastatic lesions were treated with stereotactic body RT (SBRT; 50 Gy in 4 fractions) if clinically feasible or with traditionally fractionated RT (45 Gy in 15 fractions) if not. The primary end point was the best out-of-field lesion response, and a key secondary end point was progression-free survival (PFS).

Welsh J, *et al. J Immunother Cancer* 2020;**8**:e001001. doi:10.1136/jitc-2020-001001



PEMBRO RT

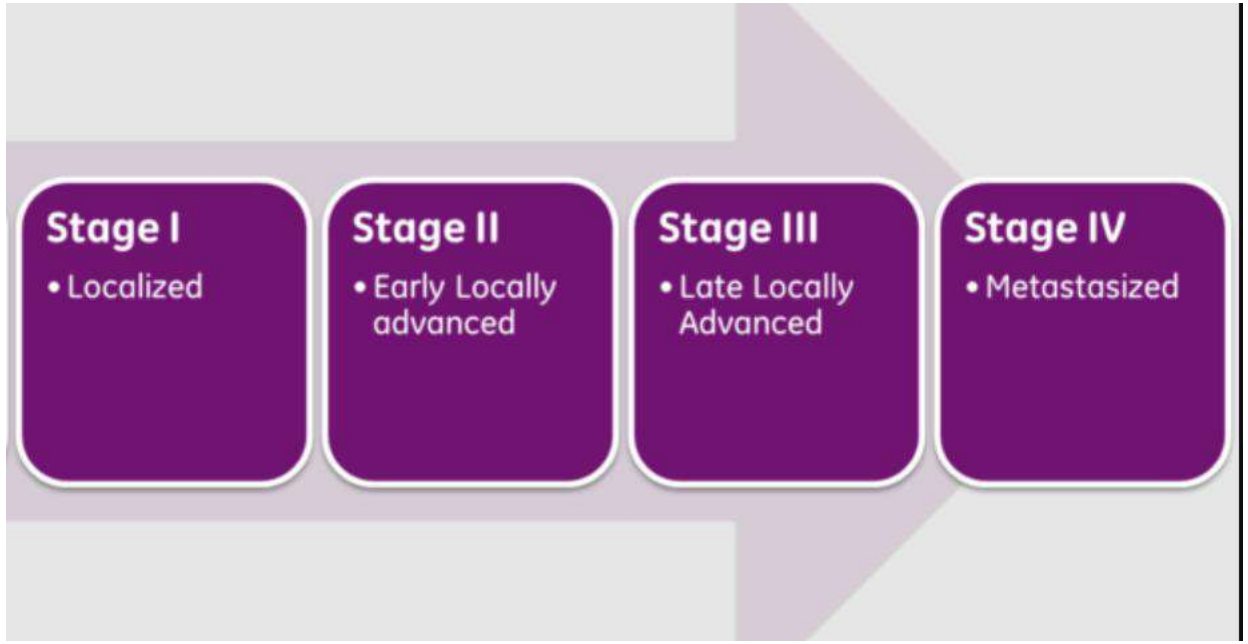
- previously treated
- IT naive
- SEQ- 1 week after last dose of RT
  DOSE- 24/3
- Single lesion, thoracic

MDACC

- both new and old
- IT naive
- CONC
- 50/5, 45/15
- multiple- liver and lung

- stage
- timing and sequencing
- dose fractioionation
- site and number of targets
- response assesment
- toxicities

Staging???


Stage I
• Localized
Stage II
• Early Locally advanced
Stage III
• Late Locally Advanced
Stage IV
• Metastasized

Safety and Efficacy of PD-1/PD-L1 inhibitors combined with radiotherapy in patients with non-small-cell lung cancer: a systematic review and meta-analysis

Cancer Medicine. 2021;10:1222–1239.

20 trials with 2027 p
stage III and 1V pat
coventional and hyp

Compared with non-combination therapy, combination therapy using PD-1/PD-L1 inhibitors and RT was associated with prolonged overall survival (OS) (1-year OS: odds ratio [OR] 1.77, 95% confidence interval [CI] 1.35–2.33, $p = 0.000$; 2-year OS: OR 1.77, 95% CI 1.35–2.33, $p = 0.000$) and progression-free survival (PFS) (0.5-year PFS: OR 1.83, 95% CI 1.13–2.98, $p = 0.014$; 1-year PFS: OR 2.09, 95% CI 1.29–3.38, $p = 0.003$; 2-year PFS: OR 2.47, 95% CI 1.13–5.37, $p = 0.023$). Combination therapy also improved the objective response rate (OR 2.76, 95% CI 1.06–7.19, $p = 0.038$) and disease control rate (OR 1.80, 95% CI 1.21–2.68, $p = 0.004$). This meta-analysis showed that compared with non-combination therapy, combination therapy using PD-1/PD-L1 inhibitors and RT did not increase the serious adverse event rates

Table 1 Summary of select ongoing trials of immunotherapy and radiation therapy for early-stage and locally advanced lung cancer

Phase	Population	Immunotherapy	Radiation dose and fractions	Status (as of May 2020)
1/2	Early-stage NSCLC	Avelumab	12 Gy × 4 or 10 Gy × 5	Active, not recruiting
1/2	Early-stage NSCLC	Nivolumab	18 Gy × 3 or 11 Gy × 5	Active, not recruiting
1/2	Early-stage NSCLC	Durvalumab	18 Gy × 3, 12.5 Gy × 4, or 6.5 Gy × 10	Recruiting
2	Early-stage NSCLC	Nivolumab	BED > 100	Recruiting
3	Early-stage NSCLC	Durvalumab	Standard-of-care SBRT	Recruiting
3	Early-stage NSCLC	Pembrolizumab	45–54 Gy in 3–5 fx	Recruiting
2	Stage I–IIA or recurrent NSCLC	Nivolumab	12.5 Gy × 4 or 7 Gy × 10	Recruiting
2	Stage IIIA NSCLC, resectable	Durvalumab and tremelimumab	1.8 Gy × 25	Recruiting
2	Stage III NSCLC, unresectable	Atezolizumab	Standard-of-care chemoradiation	Active, not recruiting
3	Stage III NSCLC, unresectable	Durvalumab	Standard-of-care chemoradiation	Active, not recruiting

Table 2 Summary of select ongoing trials of combined immunotherapy and radiation therapy for metastatic lu

Phase	Population	Immunotherapy	Radiation dose and fractions	Status (as of May 2020)
1/2	Metastatic NSCLC	Nivolumab, pembrolizumab, or atezolizumab	8–15 Gy × 3 or 6–10 Gy × 5	Active, not recruiting
2	Advanced or metastatic (stage III-IV) NSCLC	FLT3 ligand (CDX-301)	34 Gy × 1, 18 Gy × 3, or 10 Gy × 5	Active, not recruiting
1/2	Metastatic NSCLC	Ipilimumab and nivolumab	6 Gy × 5	Active, not recruiting
1	Metastatic NSCLC	Ipilimumab and nivolumab	Unspecified 3–5 fraction SBRT	Recruiting
2	Metastatic NSCLC	ADV/HSV-tk, nivolumab	6 Gy × 5	Recruiting
1	Metastatic NSCLC	Avelumab	10 Gy × 5	Recruiting

Timing & sequencing..

- All current evidence is for sequential therapy
- SBRT prior to Immunotherapy
- COLD to HOT conversion- TIL / PDL 1
- Heffich et al- TIL kinetics- 24Gy /2 sessions

TIL ↑↑ -- 5 to 8 days after RT

TREG cells ↑↑- day 10 - 16

currently concurrent ITCT- applicable to SBRT??

Metastases-directed stereotactic body radiotherapy in combination with targeted therapy or immunotherapy: systematic review and consensus recommendations by the EORTC–ESTRO OligoCare consortium

www.thelancet.com/oncology Vol 24 March 2023

- 910 patients, 32 studies

	Head and neck	Thorax	Abdomen	Bone	Body
Immune checkpoint inhibitors					
Anti-CTLA-4	..	145	86	12	13
Anti-PD-L1 and anti-PD-1	3	375	276	147	29
Anti-PD-L1 plus anti-CTLA-4 or anti-PD-1 plus anti-CTLA-4	..	38	12	12	..

Table 1: Systematic review with total number of SBRT-treated metastases per targeted agent group and anatomical location of SBRT-treated metastases

	Head and neck	Thorax	Abdomen	Bone	Body
Immune checkpoint inhibitors					
Anti-CTLA-4	..	12%	10%	8%	23%
Anti-PD-L1 and anti-PD-1	0%	6%	5%	1%	3%
Anti-PD-L1 plus anti-CTLA-4 or anti-PD-1 plus anti-CTLA-4	..	26%	0%	8%	..

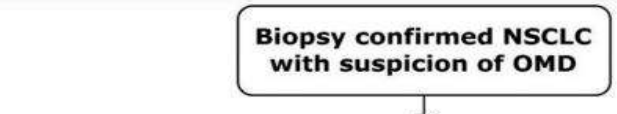
Table 2: Percentage of systematic review with severe in-field toxicity events (toxicity ≥grade 3) per SBRT treated lesion by targeted agent group and anatomical location of SBRT-treated metastases

- expert consensus-
- no consensus reached, but opined against concurrent IT
- IT can be delivered without ommision of number of cycles as scheduled
- No consensus reached regarding minimum interval between IT and SBRT
- Unchanged protocols for dose fractionation for SBRT

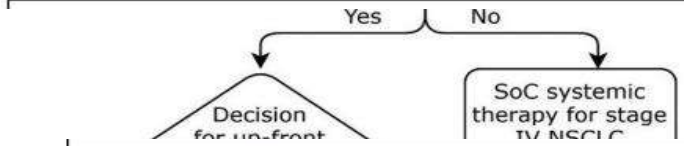
Multisite SBRT - PARADIGM SHIFT!!!!

Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline

Practical Radiation Oncology: ■■ 2023



4. For patients with oligometastatic NSCLC, deciding between RT and surgery as the definitive local treatment modality should: • Favor RT when multiple organ systems are being treated • Favor RT when the clinical prioritization is to minimize breaks from systemic therapy • Favor surgery when large tissue sampling is needed for molecular testing, to guide systemic therapy.	Strong	Expert Opinion



5. For patients with oligometastatic NSCLC, definitive local RT should use doses and fractionations which achieve durable local control. Implementation remarks: ○ Durable local control defined as minimum 85% local control at 2 years. ○ Higher BED[10] (typically >75 Gy) with SBRT alone is associated with optimal local control. ○ Lower BED[10] (50-75 Gy range) is associated with acceptable local control, typically in the setting of combination systemic therapy and SBRT.	Strong	High 9,10,36,55,68-70

Dose fractionation

Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline

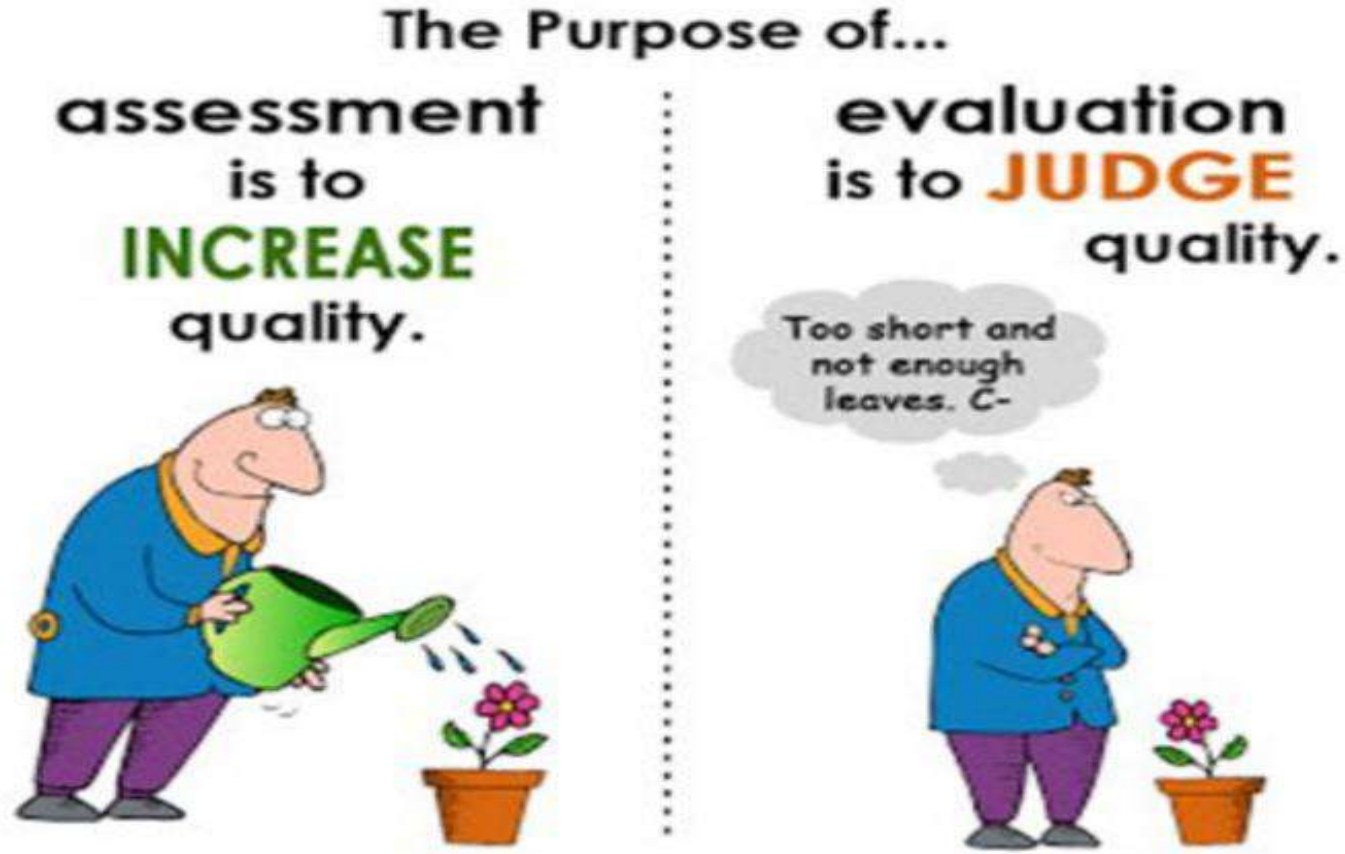
Practical Radiation Oncology: ■■ 2023

5. For patients with oligometastatic NSCLC, definitive local RT should use doses and fractionations which achieve durable local control. Implementation remarks: ○ Durable local control defined as minimum 85% local control at 2 years. ○ Higher BED[10] (typically >75 Gy) with SBRT alone is associated with optimal local control. ○ Lower BED[10] (50-75 Gy range) is associated with acceptable local control, typically in the setting of combination systemic therapy and SBRT.	Strong	High 9,10,36,55,68-70

DOSE	x FRACTIONS
15-20Gy	3
12	4
10-12	5


BENEFIT
RISK

Follow up


The Purpose of...
assessment is to INCREASE quality.
evaluation is to JUDGE quality.
Too short and not enough leaves. C-

iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics

	RECIST 1.1	iRECIST
Definitions of measurable and non-measurable disease; numbers and site of target disease	Measurable lesions are ≥10 mm in diameter (≥15 mm for nodal lesions); maximum of five lesions (two per organ); all other disease is considered non-target (must be ≥10 mm in short axis for nodal disease)	No change from RECIST 1.1; however, new lesions are assessed as per RECIST 1.1 but are recorded separately on the case report form (but not included in the sum of lesions for target lesions identified at baseline)
Complete response, partial response, or stable disease	Cannot have met criteria for progression before complete response, partial response, or stable disease	Can have had iUPD (one or more instances), but not iCPD, before iCR, iPR, or iSD
Confirmation of complete response or partial response	Only required for non-randomised trials	As per RECIST 1.1
Confirmation of stable disease	Not required	As per RECIST 1.1
New lesions	Result in progression; recorded but not measured	Results in iUPD but iCPD is only assigned on the basis of this category if at next assessment additional new lesions appear or an increase in size of new lesions is seen (≥5 mm for sum of new lesion target or any increase in new lesion non-target); the appearance of new lesions when none have previously been recorded, can also confirm iCPD
Independent blinded review and central collection of scans	Recommended in some circumstances —eg, in some trials with progression-based endpoints planned for marketing approval	Collection of scans (but not independent review) recommended for all trials
Confirmation of progression	Not required (unless equivocal)	Required
Consideration of clinical status	Not included in assessment	Clinical stability is considered when deciding whether treatment is continued after iUPD

PREDICTIVE BIOMARKERS

PDL 1
TILS
TMB
MSI
MMR

RADIOMICS
PET
MR

NLR
ctDNA
CTC


OUR
EXPERIENCE

Comparison of Response and Survival in Patients of Metastatic Non-Small-Cell Lung Cancer Receiving SBRT and Concurrent Immunotherapy-SBRT

Purpose/Objective(s): SBRT has been established as an effective modality for local control of primary, oligometastatic lung cancer. Understanding the tumor micro-environment and molecular markers have resulted in immunotherapeutic modalities that further enhance this response by 20%. In the current study we have assessed response and survival in metastatic NSCLC between groups that received SBRT and I-SBRT.

Materials/Methods: Prospectively, 25 patients with metastatic/recurrent NSCLC recruited between Jan 2017 to Feb 2020, who underwent SBRT and systemic treatment were included in the study. All patients underwent PETCT and MRI based SBRT to a dose of 30−40Gy in 5 fractions to the primary and all possible metastatic sites. Of this, 13 patients underwent ISBRT, regardless of PDL-1 status, with the 1st cycle of Pembrolizumab (n = 4) or Nivolumab (n = 9) followed by SBRT followed by adjuvant immunotherapy. Treatment response was assessed using FDG PETCT and MRI 3 monthly using the RECIST, or iRECIST 1.1 criteria depending on the group. PFS and OS were assessed

Results: Among 25 patients of histologically proven NSCLC the distribution of characteristics and outcomes is seen in Table 1. Although the characteristics of the two groups entering the study were similar, two immunotherapy related deaths were observed. Toxicities were higher in ISBRT group. PFS (p = 0.464) and OS (p = 0.689) were not significant between groups. There has been no progression in any irradiated sites for

Abstract 2325; Table Patient characteristics and outcomes

	SBRT (n = 12)	ISBRT (N = 13)
Males	5 (41.7%)	10 (71.4%)
Median Age (yrs)	62yrs (42-78)	66yrs (39-76yrs)
Morphology	Adenoca = 11 (95.6%) SCC = 1 (8.33%)	Adenoca = 10 (76.9%) SCC = 3 (23.07%)
Metastatic Sites per case (Median, Range)	4 (1-4)	3 (1-5)
Total Irradiated Sites	33	39
Brain Mets	3 (25%)	5 (38.46%)
EGFR +ve	n = 4	n = 3 (23.07%)
Immunotherapy Cycles (Median)	0	5 Cycles
Treatment Related Serious Adverse Events	0	n = 2 (15.39%)
Toxicity	0	Pneumonitis (II, III) = 3 Thyroiditis = 3 Dry Skin = 3 Fatigue = 5
Response	PD = 7 SD = 1 PR = 4 CR = 0	PD = 3 SD = 2 PR = 6 CR = 0
ORR	5 (41.67%)	8 (61.54%)
Follow up (months) (Median, Range)	5 (1-22)	5 (3-20)
Mean Progression Free Survival (months)	5.16 CI [4.44-5.88]	9.22 CI [5.69-12.75]
Mean Overall Survival (months)	25.93 CI [16.80 — 35.06]	33.83 CI [15.9 — 51.7]

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Understanding the Immune Profile of SBRT – Could It Evolve Into Becoming A Surrogate Biomarkers To Treatment Response

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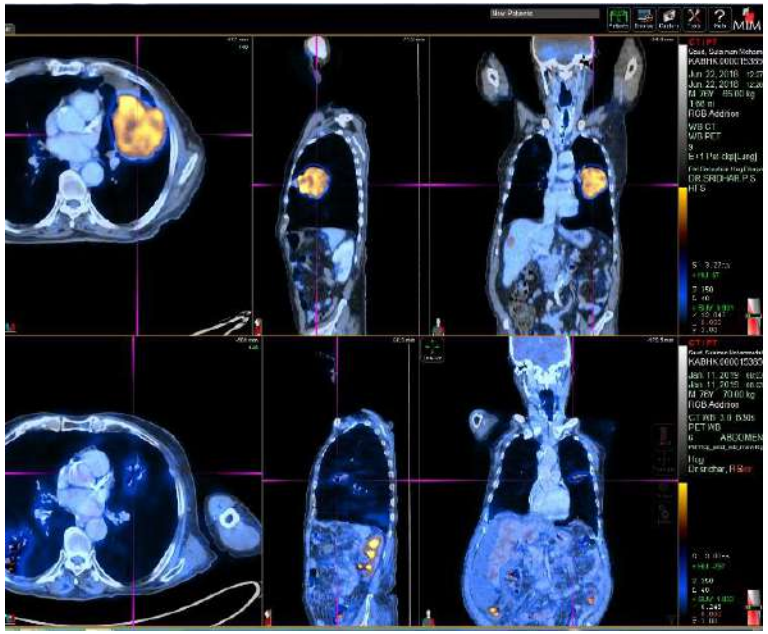
Show all authors DOI: https://doi.org/10.1016/j.ijrobp.2020.07.1598 • Check for updates

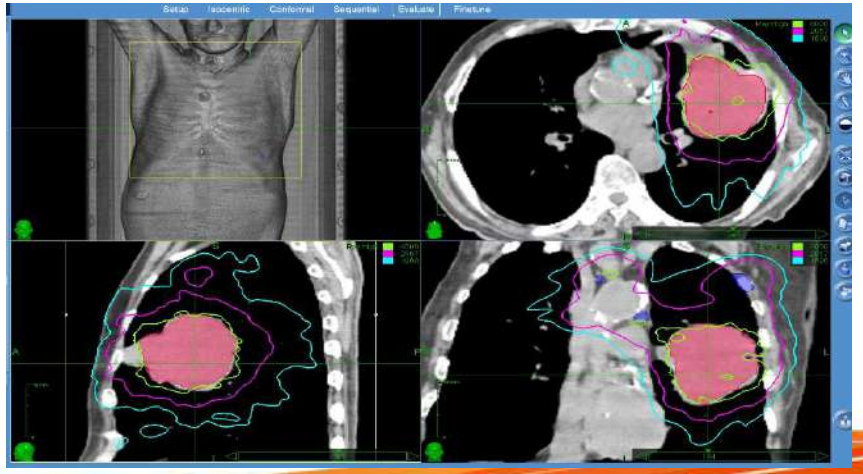
Abstract 3151; Table

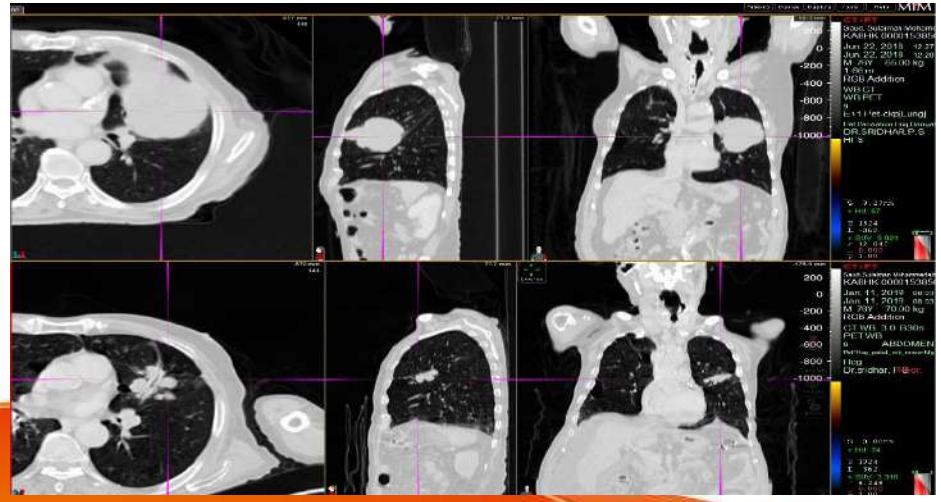
Marker	Measure	Pre SBRT	Post SBRT	P value
TNF – Alpha	Median (Q1, Q3)	0.539 (0.265,0.745)	1.129 (0.520,3.403)	0.001
N = 19	Min, Max	0.047, 11.878	0.116, 12.912	
INF-Gamma	Median (Q1, Q3)	0.423 (0.160,0.870)	0.510 (0.245,1.498)	0.046
N = 22	Min, Max	0.002, 1.729	0.021, 4.645	
IL-10	Median (Q1, Q3)	0.020 (0.001, 0.058)	0.026 (0.006,0.078)	0.733
N = 22	Min, Max	-0.011, 0.537	-0.006, 0.121	
TGF-Beta	Median (Q1, Q3)	0.067 (0.035,0.101)	0.068 (0.036,0.10)	0.638
N = 22	Min, Max	0.007, 0.271	0.019, 0.167	
TGF-Beta/IFN-Gamma	Median (Q1, Q3)	0.182 (0.069,0.359)	0.1343 (0.019,0.350)	0.189
	Min, Max	0.01, 65.65	0, 6.21	

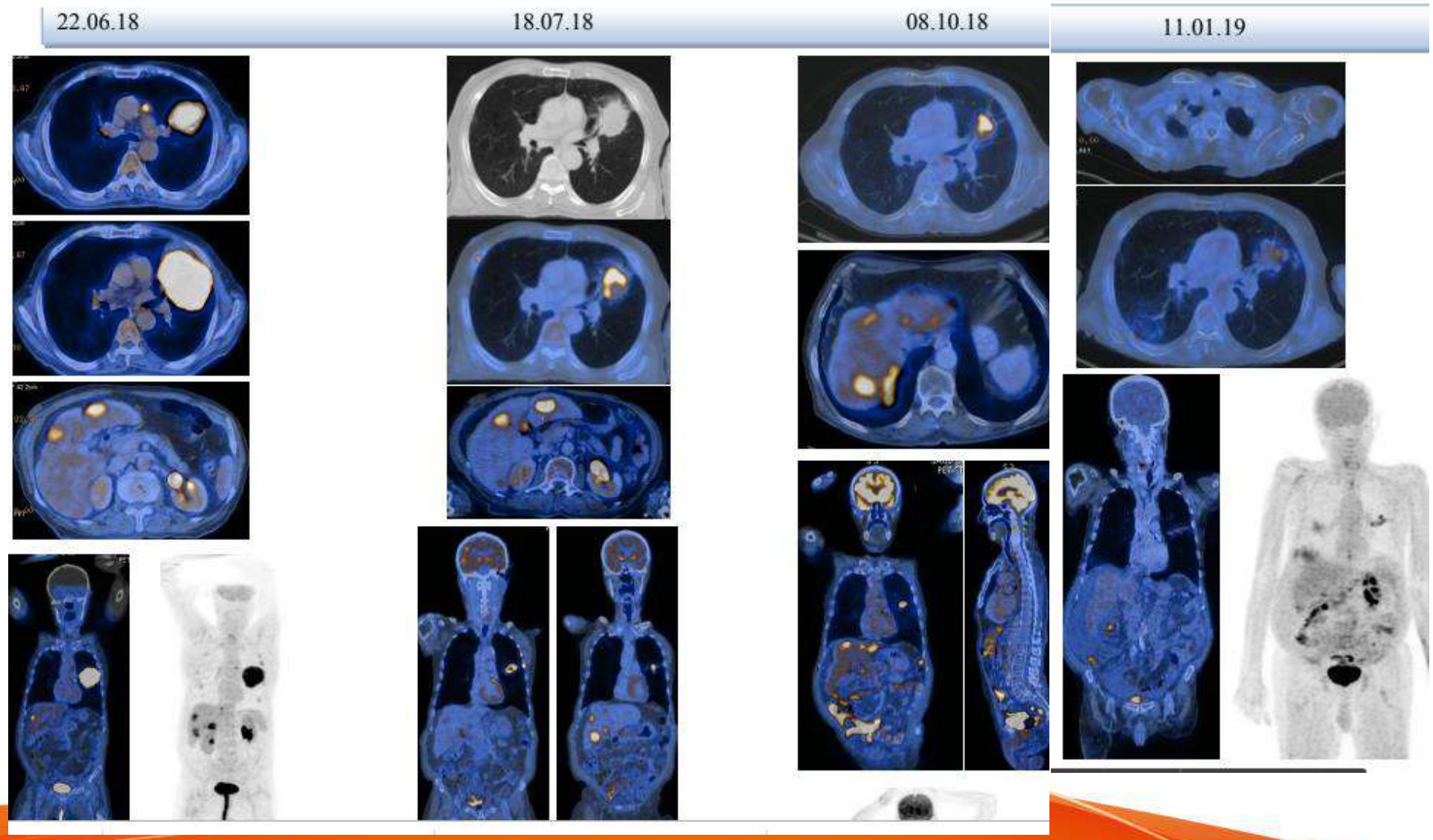
Conclusion: Our current study showed a significant elevation in immune markers post SBRT. The increase in IFN-Gamma, being indicative of T-cell activation, along with increase in TNF-Alpha suggested an increase in pro-inflammatory activity in PBMCs. The ratio of IFN-Gamma to TGF-Beta is indicative of consolidated activation of the immune system considering both pro- and anti-inflammatory activity. This ratio decreased (although non-significantly) providing a hint that there might be an immunogenic effect that impacts the immune effects on the tumor.

76yrs/M/SCC/post CT/BT/CKOM-IMT





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CYBERKNIFE

- 30/05/09-30/09/22
- Total – 3192/4844
- Extracranial-1698/2673
- Intracranial-1494/2171

CNS-GLIOMA	582
BENIGN	725
HN	250
LUNG	617
GI	282
HPB	325
BREAST	440
STS	108
OVARYCX	90
PROSTATE	447
RCCBLAD	152

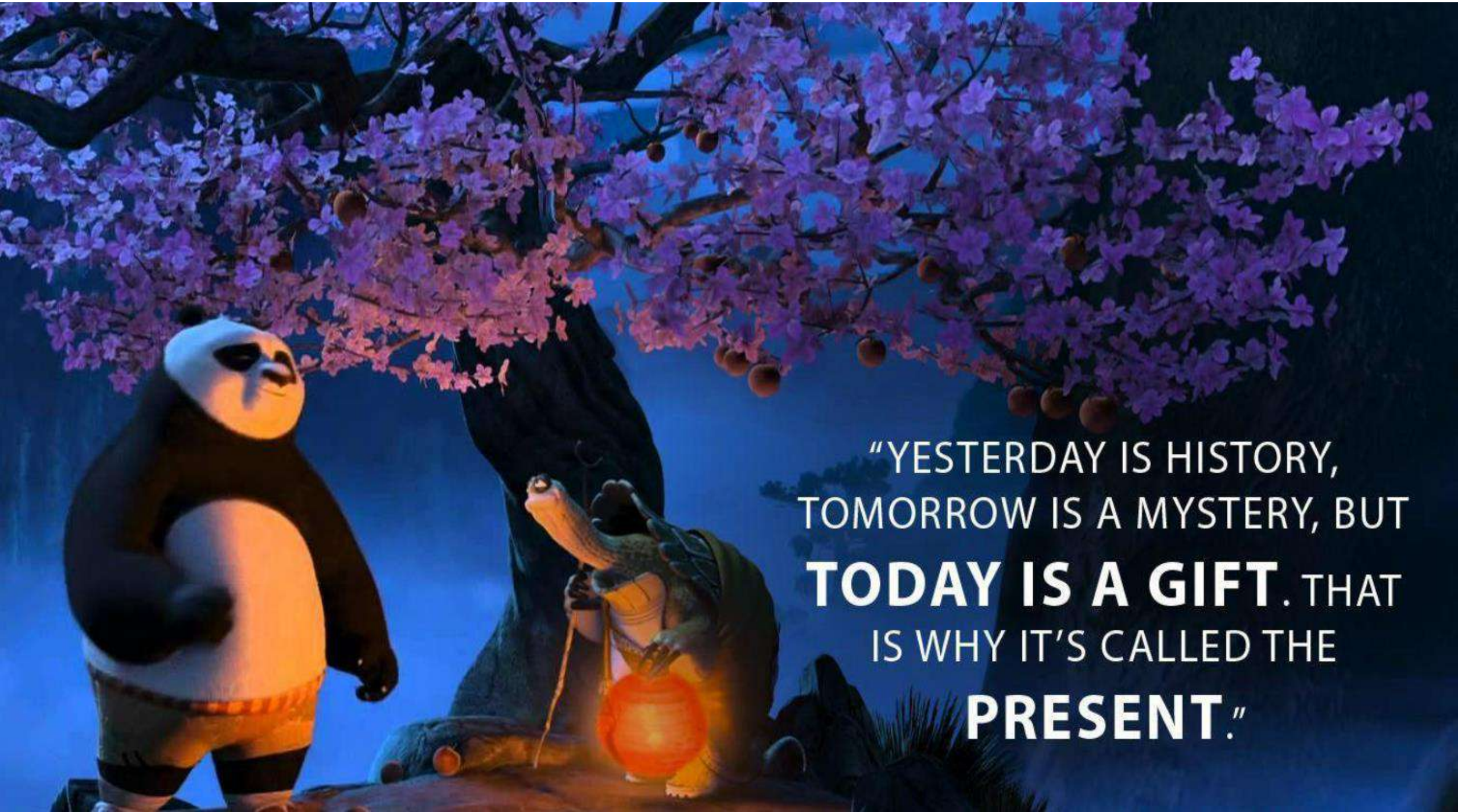
	SPS	OTHERS	TOTAL
6D SKULL	1424	736	2171
X-SPINE	625	236	865
FIDUCIALS	428	213	645
SYNCHRONY	587	405	997
X-LUNG	20	5	25

MDT-METASTATIC DIRECTED THERAPY

	SPS	OTHERS	TOTAL
BRAIN METS	286	118	508
LIVER METS	84	56	140
LUNG METS	70	47	117
SPINE METS	60	36	76
ADRENALS	20	5	25


look into
the
Future

- Immunoradiotherapy has emerged as most promising protocol for mNSCLC
- Early stage- adjuvant/sequential
- advanced(stage III)- ?? ImmunoSBRT >>> CTRT
- SBRT- “SECRET INGREDIENT”


"YESTERDAY IS HISTORY,
TOMORROW IS A MYSTERY, BUT
TODAY IS A GIFT. THAT
IS WHY IT'S CALLED THE
PRESENT."