XXV CONGRESSO NAZIONALE

AIRO 2015

PALACONGRESSI - Rimini, 7-10 novembre

Radioterapia e nuove molecole biologiche: implicazioni cliniche

Associazione Italiana Radioterapia Oncologica

Carlo Greco

Radioterapia Oncologica

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DICHIARAZIONE

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

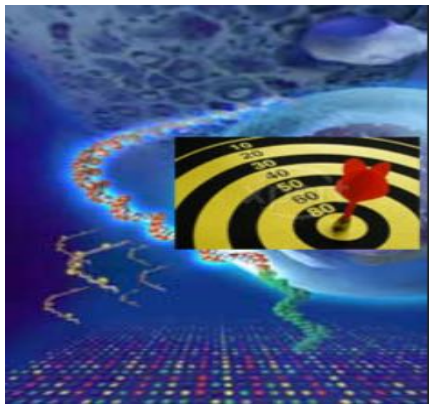
- Posizione di dipendente in aziende con interessi commerciali in campo sanitario

- Consulenza ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**

Increase tumor control

New technologies → Dose escalation

Integrated Therapies

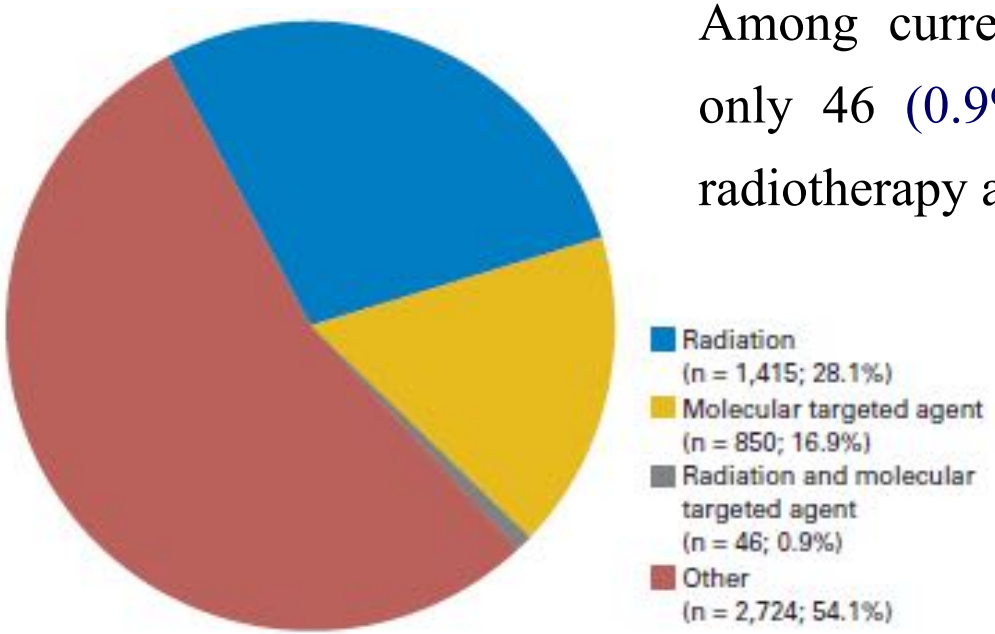


JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Interaction of Radiation Therapy With Molecular Targeted Agents

Zachary S. Morris and Paul M. Harari



Among current phase III trials for cancer, only 46 (0.9%) examine a combination of radiotherapy and molecular targeted therapy

Morris ZS, Harari PM, JCO 2014;32(28):2886-93

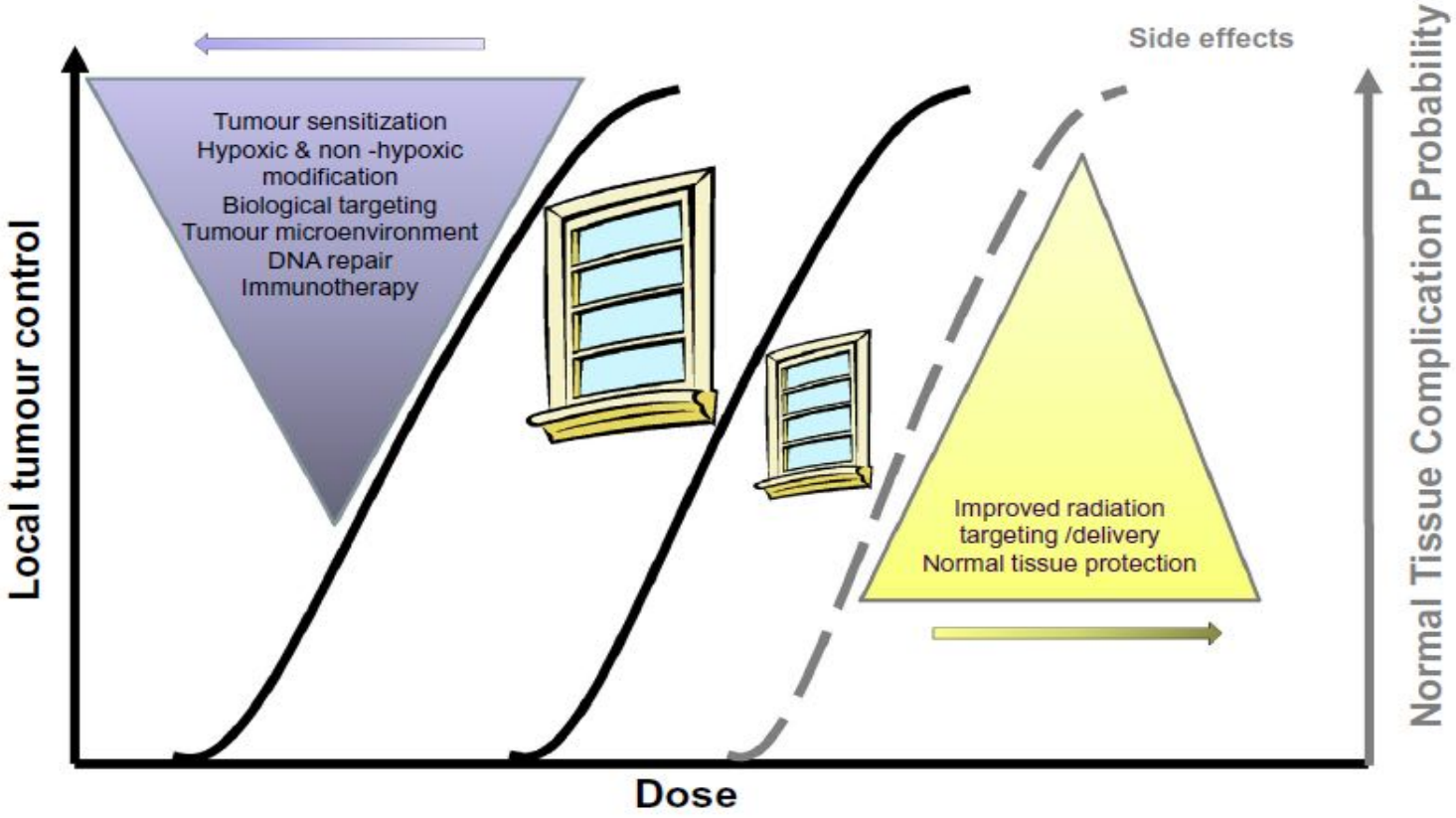
Radiotherapy and new biological molecules: clinical implications

Radiotherapy and targeted therapies

- ✓ Locally advanced disease
- ✓ Metastastic disease

Radiotherapy and Immunotherapy

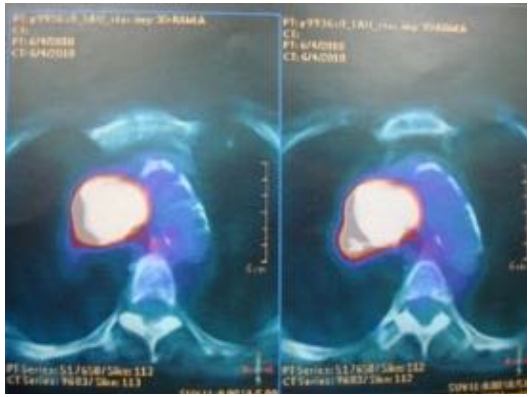
Recent advances in molecularly targeted therapies coupled with technologic strides in radiotherapy have the potential to improve outcomes for patients?



Radiotherapy and new biological molecules: clinical implications

Radiotherapy and targeted therapies

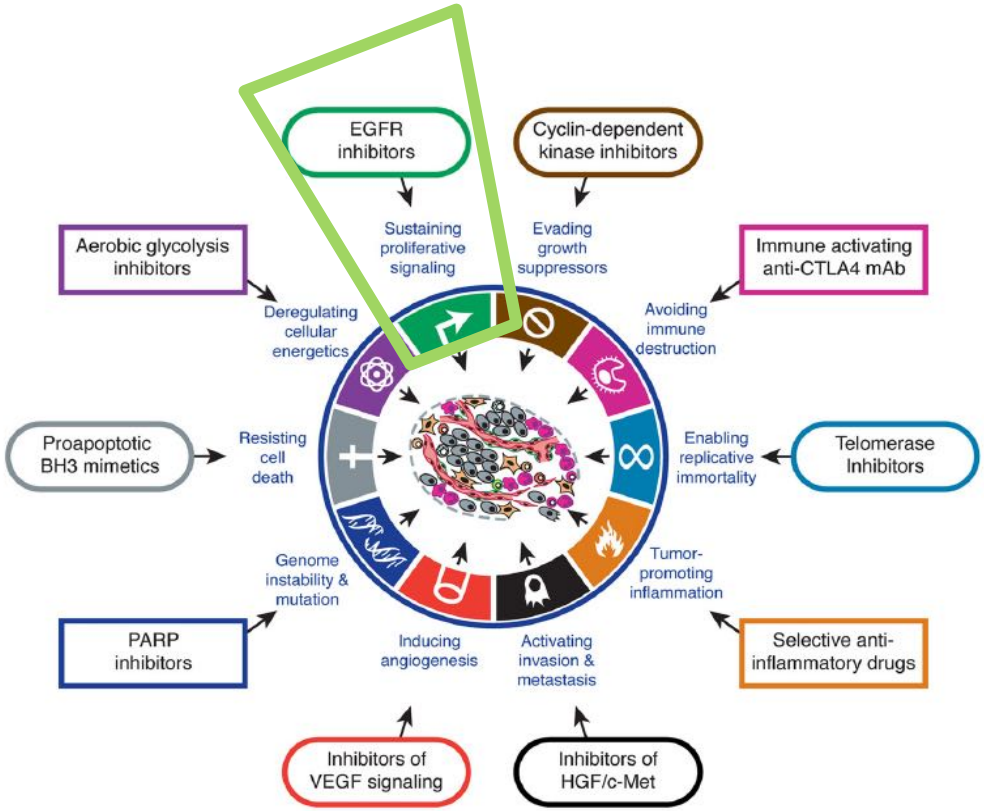
- ✓ **Locally advanced disease**
- ✓ Metastastic disease



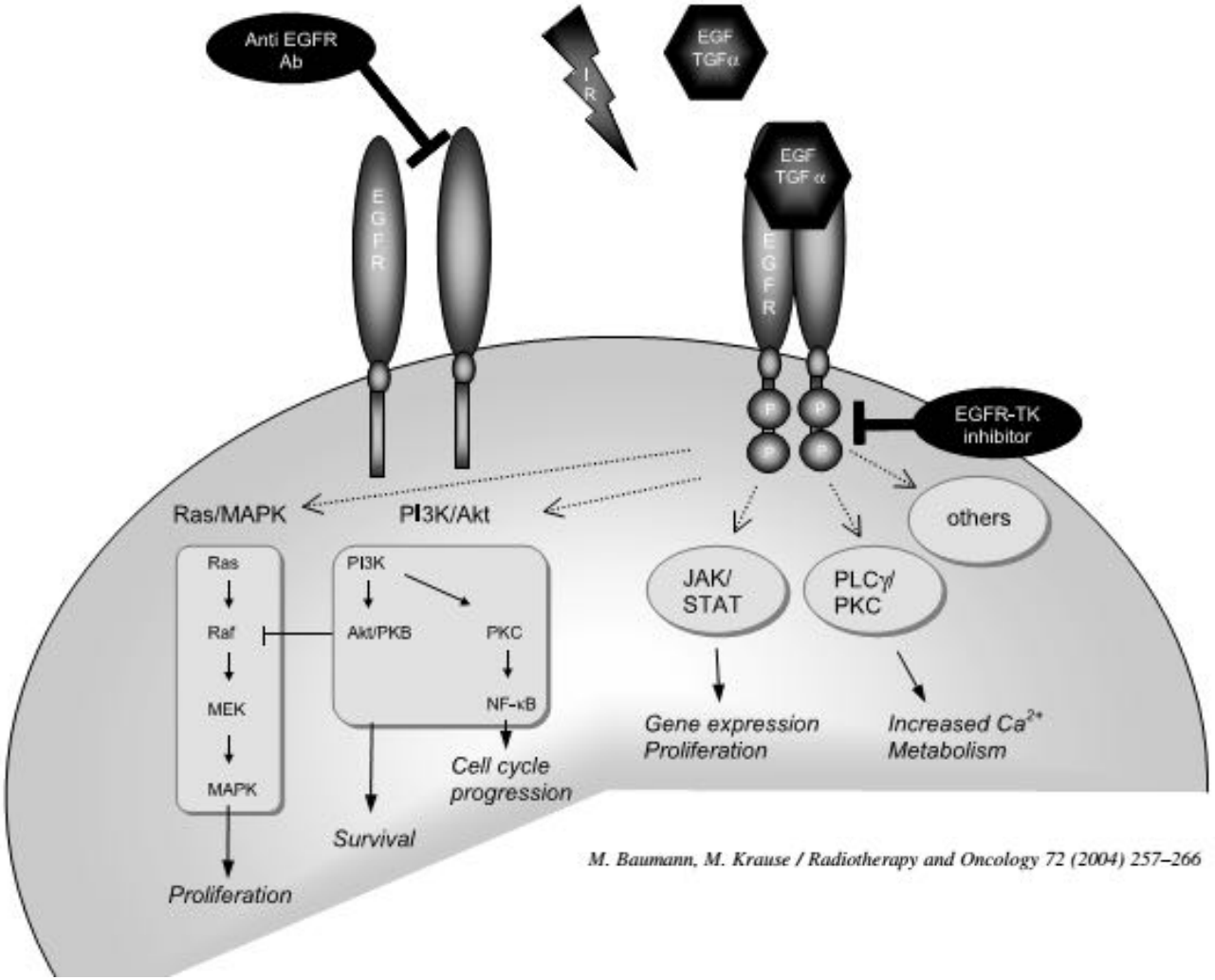
Radiotherapy and Immunotherapy

Inhibitors of EGFR signaling

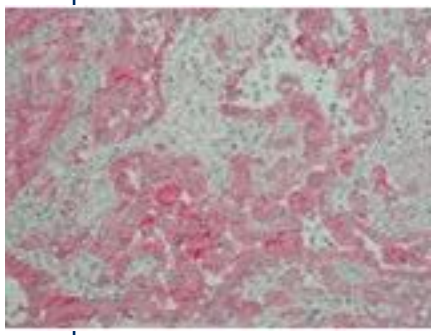
- **Preclinical Rationale**
- Clinical Experience



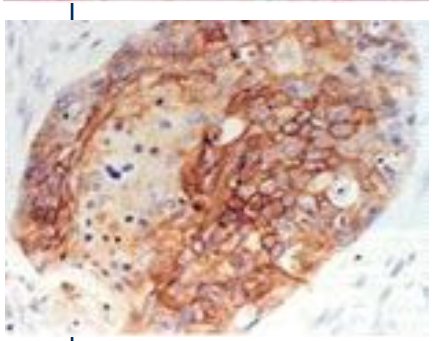
EGFR as a target for cancer treatment



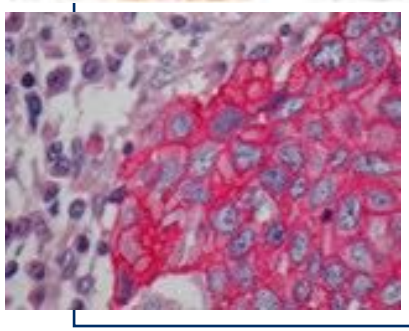
Tumors that overexpress EGFR are less responsive to Radiotherapy



colon



lung



Head and Neck

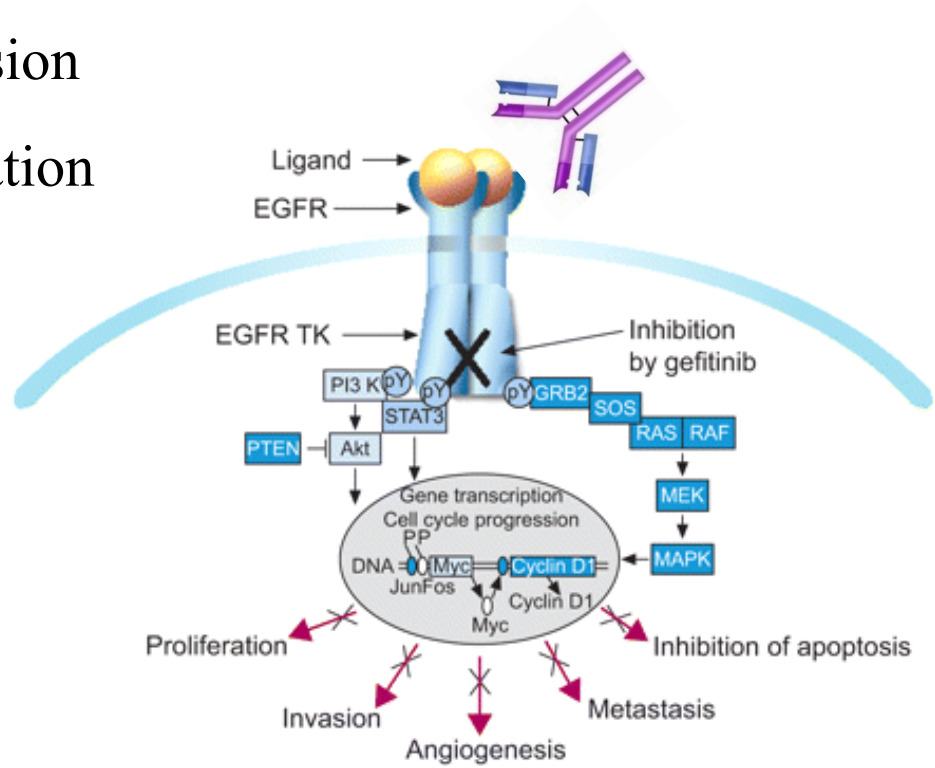
Head and Neck	80-100%
Esophageal	30–70%
Glioma	60%
NSCLC	40-80%
Pancreatic	30-89 %
Colo-Rectal	25-77%

vek K. Mehta Frontiers in Oncology 2012

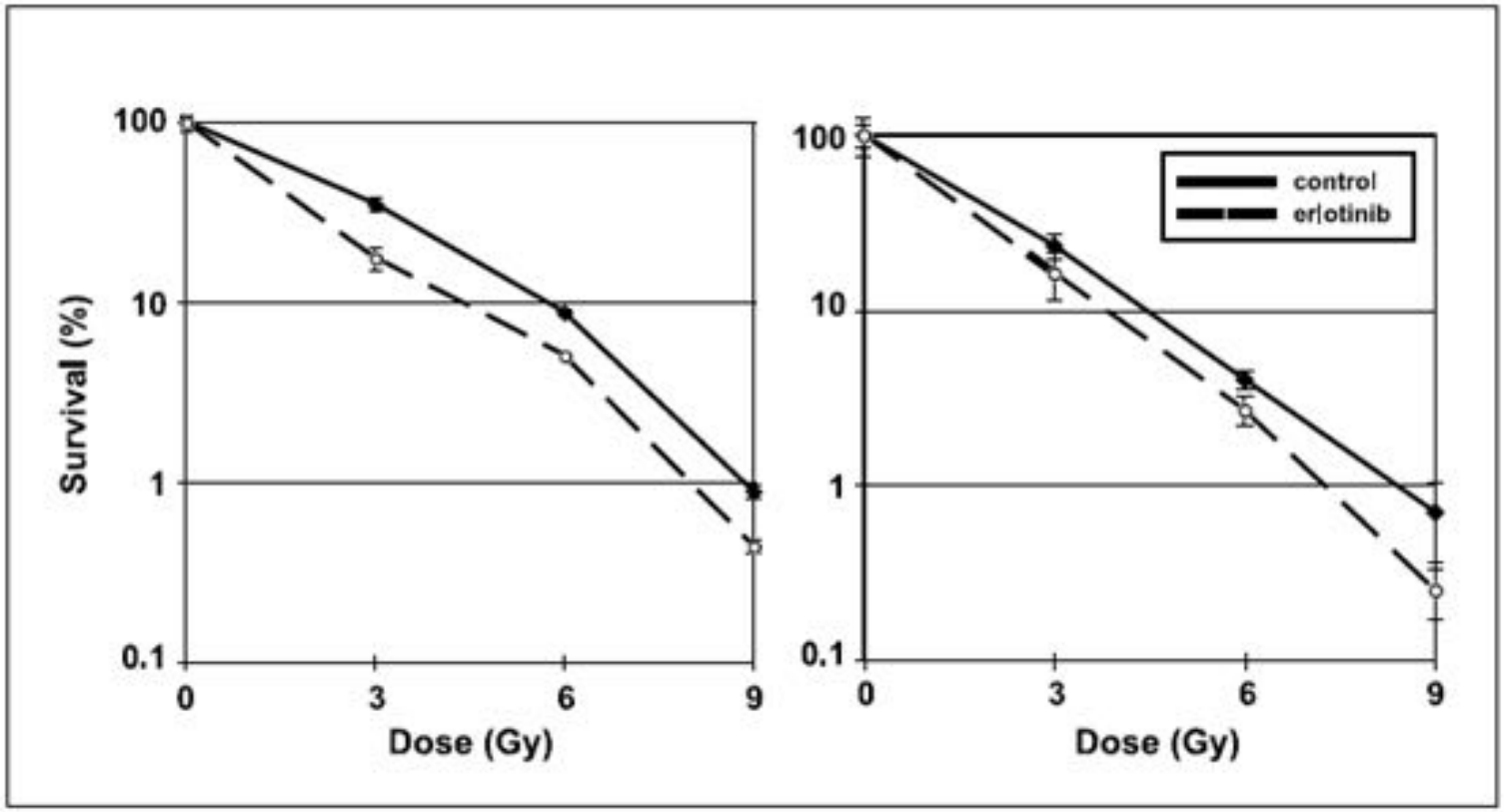
Radiotherapy and EGFR Inhibitors

Preclinical Evaluation of Mechanisms

- ✓ Inhibition of DNA repair (→apoptosis)
- ✓ Inhibition of cell cycle progression
- ✓ Inhibition of clonogen repopulation
- ✓ Angiogenesis



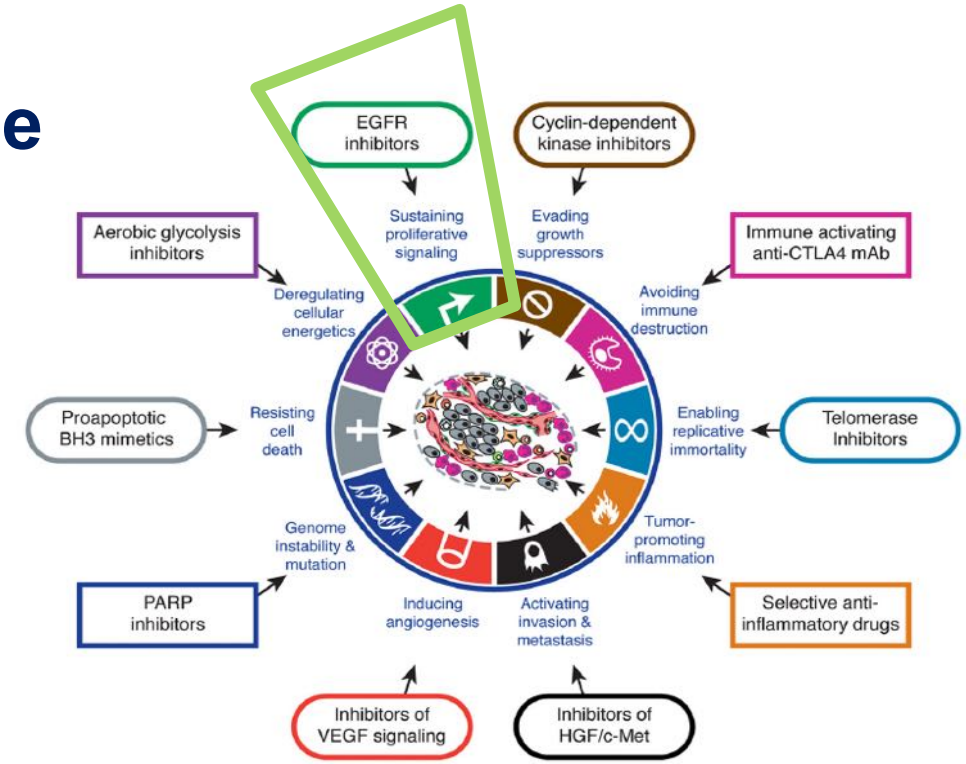
Radiosensitivity



Baumann M, Radiotherapy and Oncology, 2007; 14: 238-248

Inhibitors of EGFR signaling

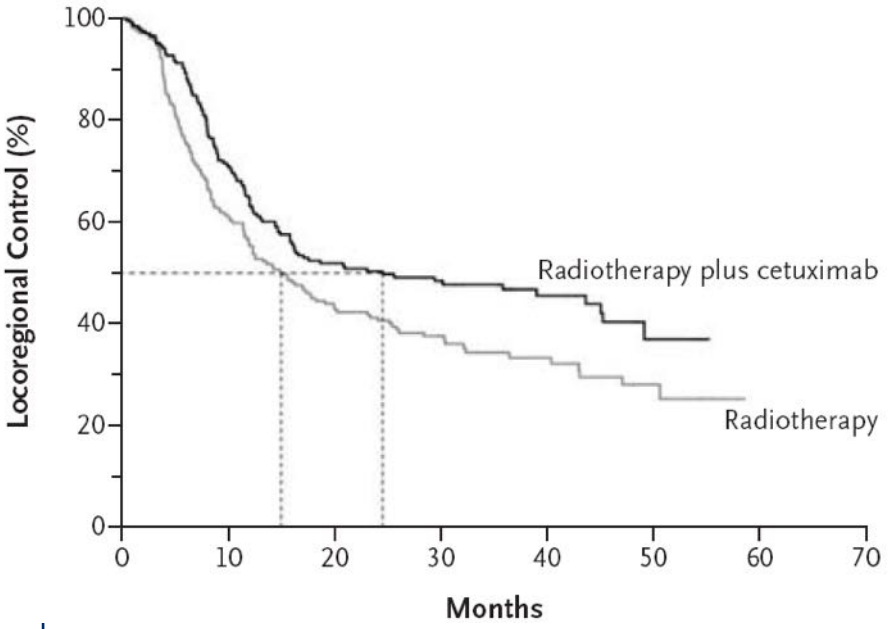
- Preclinical Rationale
- **Clinical Experience**

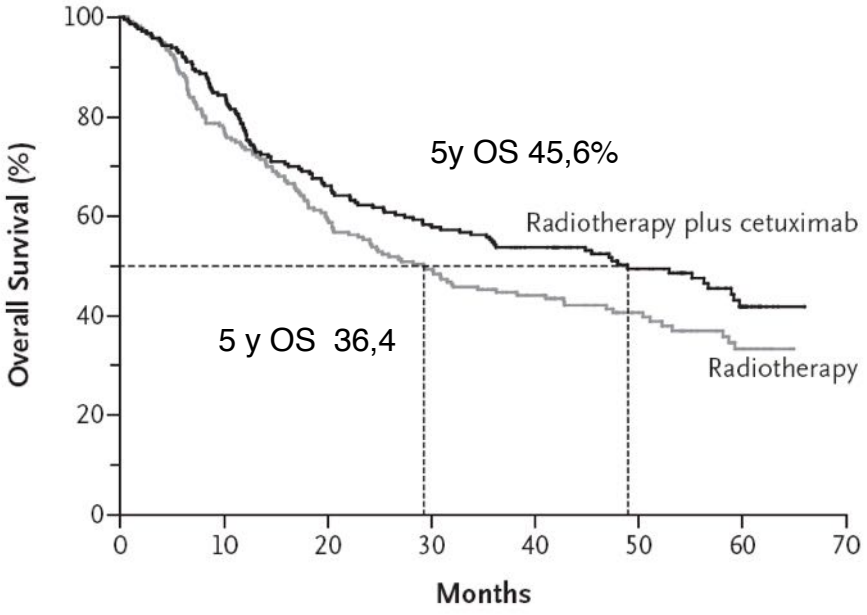


ORIGINAL ARTICLE

Radiotherapy plus Cetuximab for Squamous-Cell Carcinoma of the Head and Neck

James A. Bonner, M.D., Paul M. Harari, M.D., Jordi Giralt, M.D., Nozar Azarnia, Ph.D., Dong M. Shin, M.D., Roger B. Cohen, M.D., Christopher U. Jones, M.D., Ranjan Sur, M.D., Ph.D., David Raben, M.D., Jacek Jassem, M.D., Ph.D., Roger Ove, M.D., Ph.D., Merrill S. Kies, M.D., Jose Baselga, M.D., Hagop Youssoufian, M.D., Nadia Amellal, M.D., Eric K. Rowinsky, M.D., and K. Kian Ang, M.D., Ph.D.*





Bonner JA New Engl J Med 2006;354(6):567–78.2006/02/10.

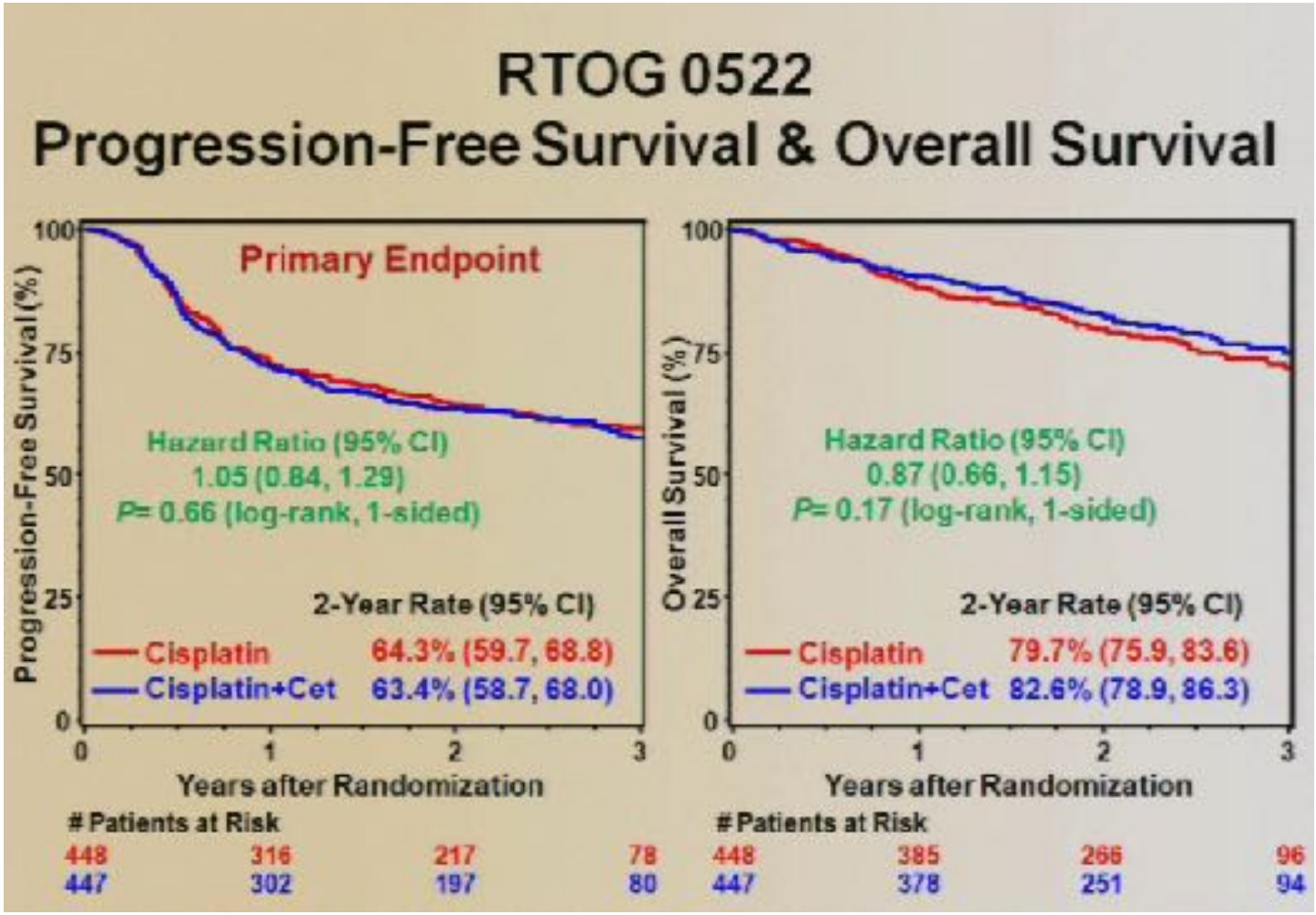
RT + chemotherapy +/- Cetuximab: RTOG phase III trial (0522)

Stage III & IV* SCC of:
- Oropharynx
- Hypopharynx
- Larynx

Stratify:
- Larynx – others
- N0–N1,2a,2b– N2c-3
- KPS
  60-80 ~ 90-100
- 3-D vs IMRT
- Pre-Rx PET (yes/no)

RANDOMIZE

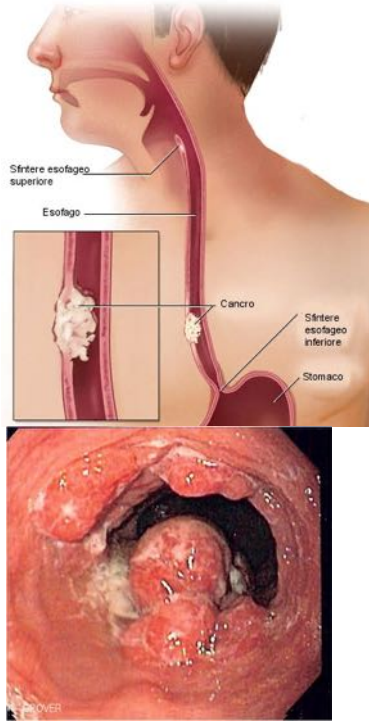
1. Accelerated FX* + CDDP: 100 mg/m², q3w x 2
2. Accelerated FX* + CDDP: 100 mg/m², q3w x 2
   ERBITUX: 400 mg/m², Pre-RT, then 250 mg/m²/w x 7


RTOG 0522
Progression-Free Survival & Overall Survival
Primary Endpoint
Progression-Free Survival (%)
Hazard Ratio (95% CI)
1.05 (0.84, 1.29)
P= 0.66 (log-rank, 1-sided)
2-Year Rate (95% CI)
Cisplatin 64.3% (59.7, 68.8)
Cisplatin+Cet 63.4% (58.7, 68.0)
Years after Randomization
Patients at Risk
448 316 217 78
447 302 197 80
Overall Survival (%)
Hazard Ratio (95% CI)
0.87 (0.66, 1.15)
P= 0.17 (log-rank, 1-sided)
2-Year Rate (95% CI)
Cisplatin 79.7% (75.9, 83.6)
Cisplatin+Cet 82.6% (78.9, 86.3)
Years after Randomization
Patients at Risk
448 385 266 96
447 378 251 94

The initial report of RTOG 0436: A phase III trial evaluating the addition of cetuximab to paclitaxel, cisplatin, and radiation for patients with esophageal cancer treated without surgery.

344 pts 2008-2013

	cCR	1 y OS	2y OS
Cetuximab	56%	64%	44%
No Cetuximab	59%	65%	42%
	p=0,72	p=0,7	



The addition of cetuximab to concurrent chemoradiation did not improves OS and cCR

RTOG 0617

A Randomized Phase III Comparison of Standard-Dose (60 Gy) versus High-Dose (74 Gy) Conformal Radiotherapy with Concurrent and Consolidation Carboplatin/Paclitaxel +/- Cetuximab in Patients with Stage IIIA/IIIB Non-Small Cell Lung Cancer

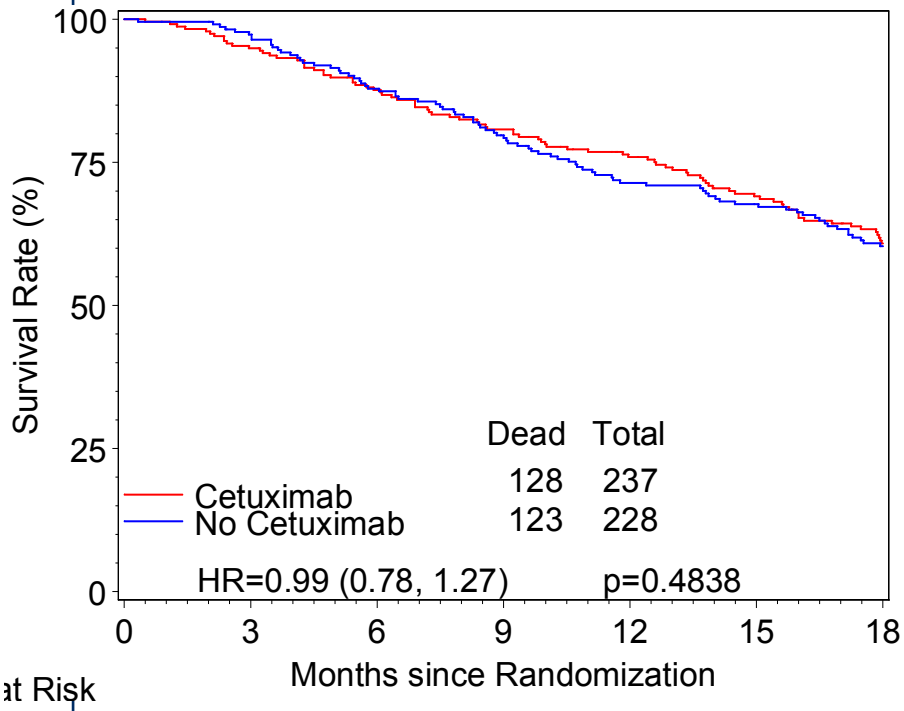
Intergroup Partecipation:

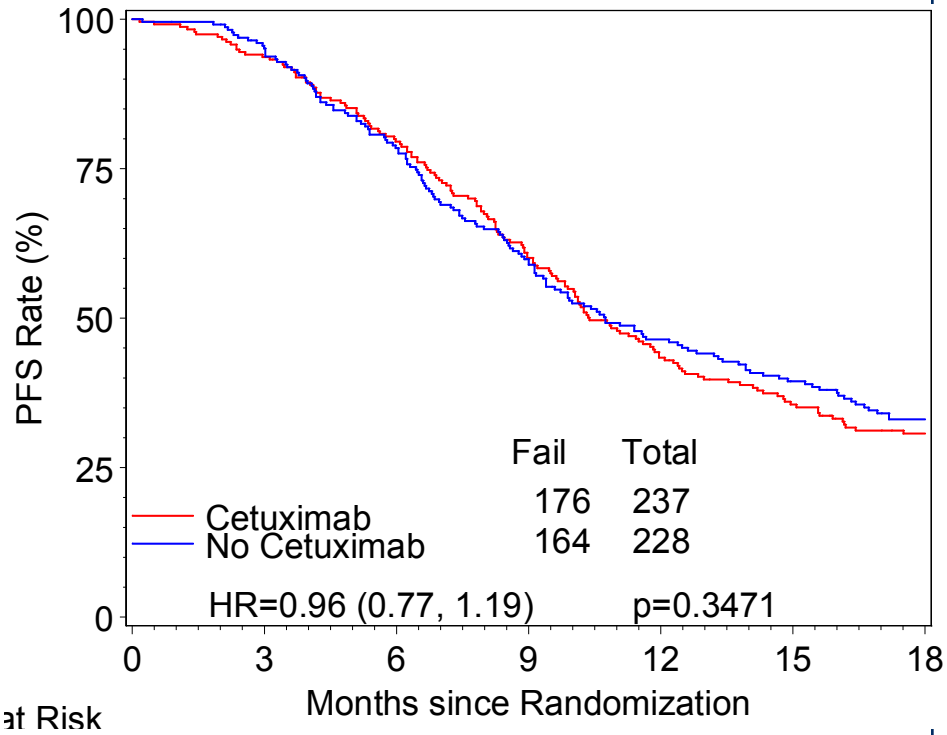
RTOG, NCCTG, CALGB

Bradley JD, Lancet Oncol 2015; 16: 187-199

STRATIFY	RANDOMIZE	Concurrent Treatment	Consolidation Treatment
RT Technique 1.3D-CRT 2.IMRT **Zubrod** 1.0 2.1 **PET Staging** 1.No 2.Yes **Histology** 1.Squamous 2.Non Squamous		**Arm A** Concurrent chemotherapy* RT to **60 Gy**, 5 x per wk for 6 wks	Arm A Consolidation chemotherapy*
		Arm B Concurrent chemotherapy* RT to **74 Gy**, 5 x per wk for 7.5 wks	Arm B Consolidation chemotherapy*
		Arm C Concurrent chemotherapy* and **Cetuximab** RT to **60 Gy**, 5 x per wk for 6 wks	Arm C Consolidation chemotherapy* and **Cetuximab**
		Arm D Concurrent chemotherapy* and **Cetuximab** RT to **74 Gy**, 5 x per wk for 7.5 wks	Arm D Consolidation chemotherapy* and **Cetuximab**

Cetuximab vs No Cetuximab





Summary of Adverse Events Definitely, Probably, or Possibly Related to Treatment (CTCAE V3.0)

Concurrent Cetuximab

	Cetuximab (n=237) Grade			No Cetuximab (n=227) Grade		
	3	4	5	3	4	5
Worst non-hematologic	130 (54.9%)	26 (11.0%)	11 (4.6%)	91 (40.1%)	18 (7.9%)	6 (2.6%)
Combined*	167 (70.5%)			115 (50.7%)		
Worst overall	117 (49.4%)	74 (31.2%)	11 (4.6%)	93 (41.0%)	57 (25.1%)	7 (3.1%)
Combined*	202 (85.2%)			157 (69.2%)		

*p<0.0001

TKIi and RT-CT

Salama and Vokes, JCO 2013; 31:1029-1038

Table 2. Selected Phase I/II Studies of Concurrent EGFR-TKI and Chemoradiotherapy for NSCLC

Study	No. of Patients	Concurrent	*EGFR* Inhibition	RT (Gy)	Ind/Consol	Adverse Events (%)		Response Rate (%)	OS			
						Esophagitis Grades 3-4	Neutropenia Grades 3-4		Median (months)	1-Year (%)	2-Year (%)	3-Year (%)
University of Chicago[44]	16	Cisplatin, etopside	Erlotinib MTD: 150 mg/d	66	Consol: docetaxel	19	50	65	11			20
	15	Carboplatin, paclitaxel	Erlotinib MTD: 150 mg/d	66	Ind: carboplatin, paclitaxel	40	20	59	15			16
CALGB 30106 (good risk)[43]	39	Carboplatin, paclitaxel	Gefitinib 250 mg/d	66	Consol: carboplatin, paclitaxel	31	38	81	13	53		
Zurich[45]	14	Cisplatin (optional)	Gefitinib 250 mg/d	66	Ind: cisplatin based	22	11	21	12.5		NS	
University of North Carolina[47]	23	Carboplatin, paclitaxel	Gefitinib 250 mg/d	74	Ind: carboplatin, paclitaxel, irinotecan	19.5	19	NS	16		20	

	N° pts	*Concurrent*	*Tox G3-4*	*Median SVV*	*Notes*
MD Anderson (Komaki 2012)	48	Carbo-Taxol	NS	26 months	Response Rate 80%
CBM (Ramella 2013)	60	Gem/Pem weekly	2-8%	23.3 months	SCC: Gem+ Erl NSCC:Pem+Erl

Recent advances in molecularly targeted therapies coupled with technologic strides in radiotherapy have the potential to improve outcomes for patients?

1. **Pre-clinical results interesting**

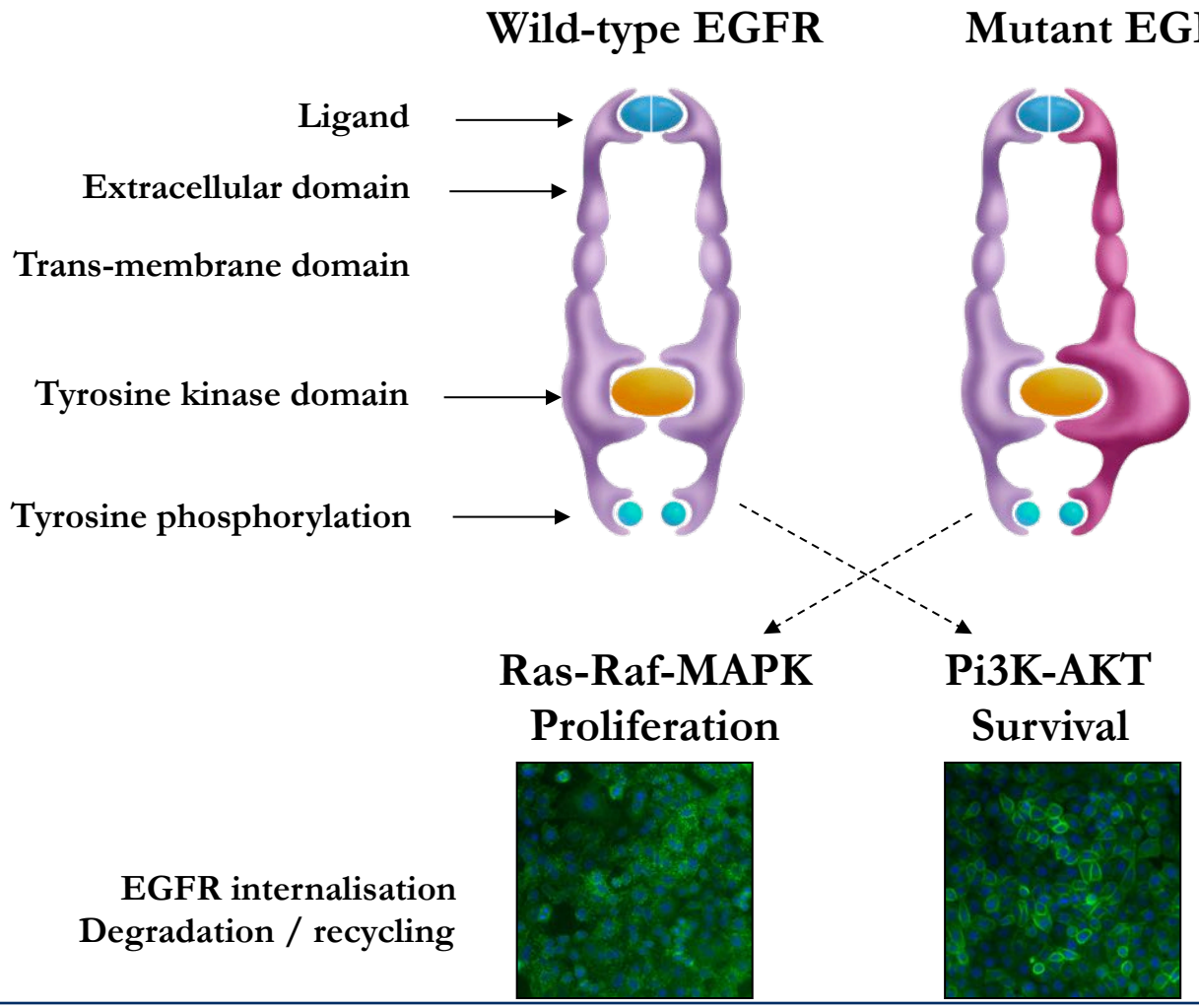
2. **Clinical: disappointing results (no standard therapy)**

How we can improve the likelihood of clinical success with target therapy?

Identify clinical variables and biomarkers that can be used for patient selection (mutational status of K-Ras and EGFR)

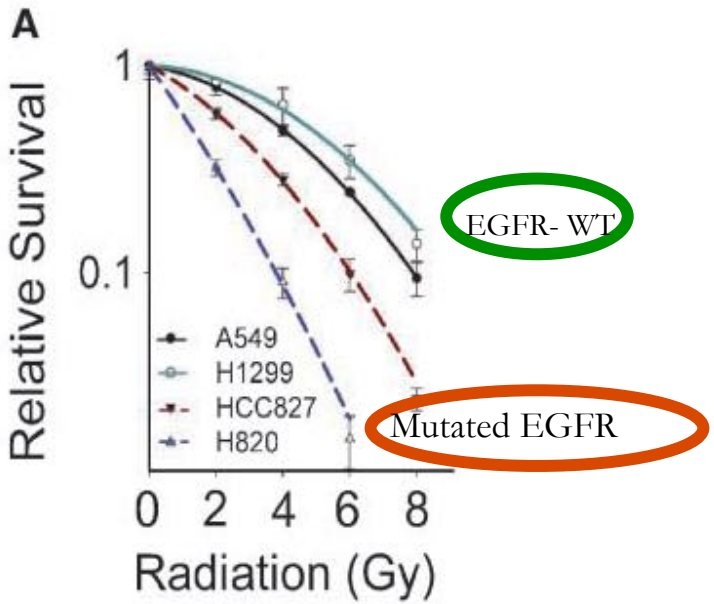
The lack of biomarkers in many drug-radiotherapy studies has been a major cause of trials failing to live up to expectations

EGFR mutation causes conformational change and increased activation



Non–Small Cell Lung Cancers with Kinase Domain Mutations in the Epidermal Growth Factor Receptor Are Sensitive to Ionizing Radiation

Amit K. Das,[1] Mitsuo Sato,[2] Michael D. Story,[1] Michael Peyton,[2] Robert Graves,[7] Stella Redpath,[7] Luc Girard,[2] Adi F. Gazdar,[2] Jerry W. Shay,[3] John D. Minna,[2,4,5,6] and Chaitanya S. Nirodi[1]



The WT EGFR cell lines showed a significant tolerance to radiation and modest loss of colony-forming ability.

The mutant EGFR-expressing NSCLC cell lines exhibited high radiosensitivity

RTOG
RADIATION THERAPY ONCOLOGY GROUP

RTOG 1306 : A RANDOMIZED PHASE II STUDY OF INDIVIDUALIZED COMBINED MODALITY THERAPY FOR STAGE III NON-SMALL CELL LUNG CANCER (NSCLC)

EGFR TK Mutation Cohort

RANDOMIZE

Arm 1: Induction Therapy:
Erlotinib, 150 mg/day for 12 weeks*

Arm 2: Concurrent †chemotherapy and radiation, 60 Gy

Concurrent †chemotherapy and IMRT or 3D-CRT 60 Gy in 30 fxs

ALK Tran L Cohort

RANDOMIZE

Arm 3: Induction Therapy:
Crizotinib, 250 mg/bid for 12 weeks*

Arm 4: Concurrent †chemotherapy and radiation, 60 Gy

Concurrent †chemotherapy and IMRT or 3D-CRT 60 Gy in 30 fxs

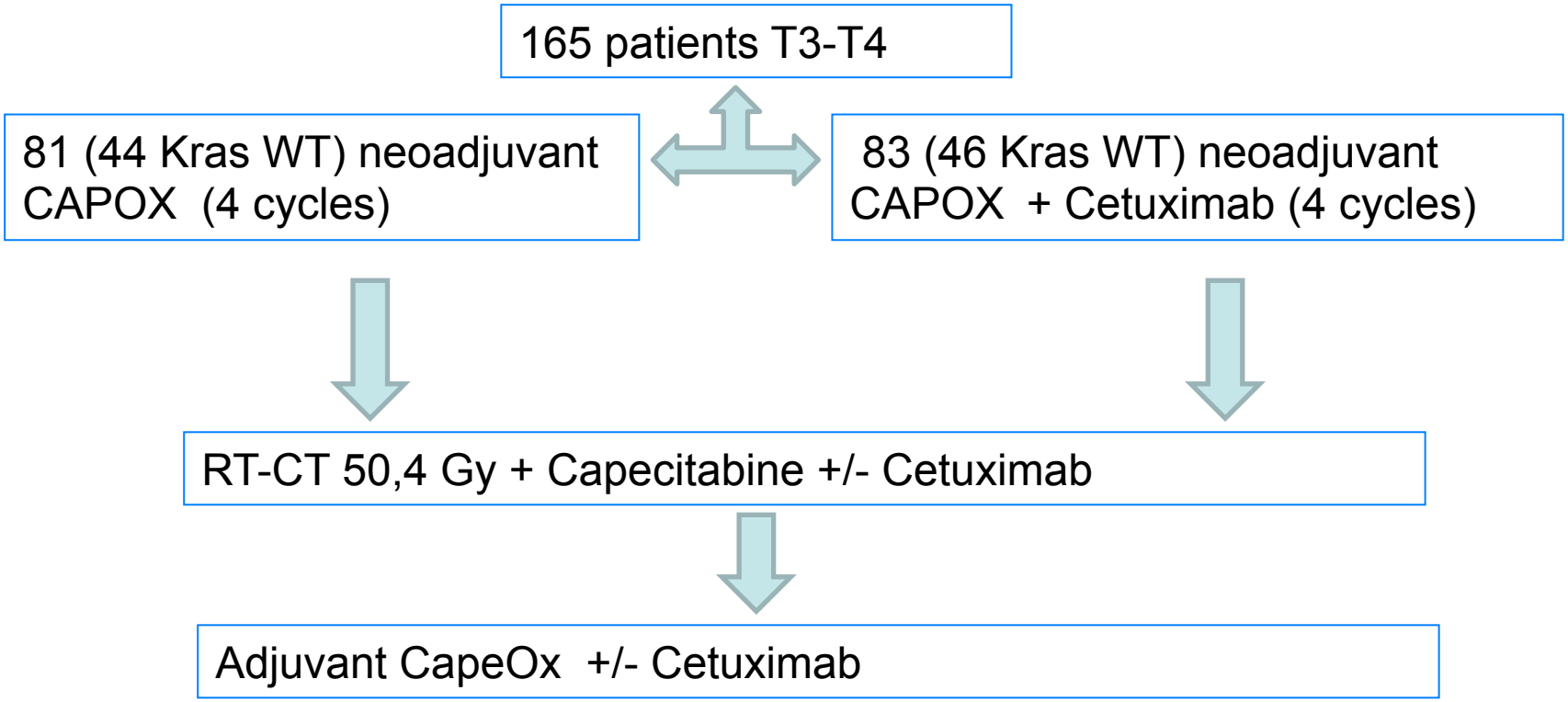
RTOG 1306, Version Date: 9/11/15

VOLUME 30 · NUMBER 14 · MAY 10 2012

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

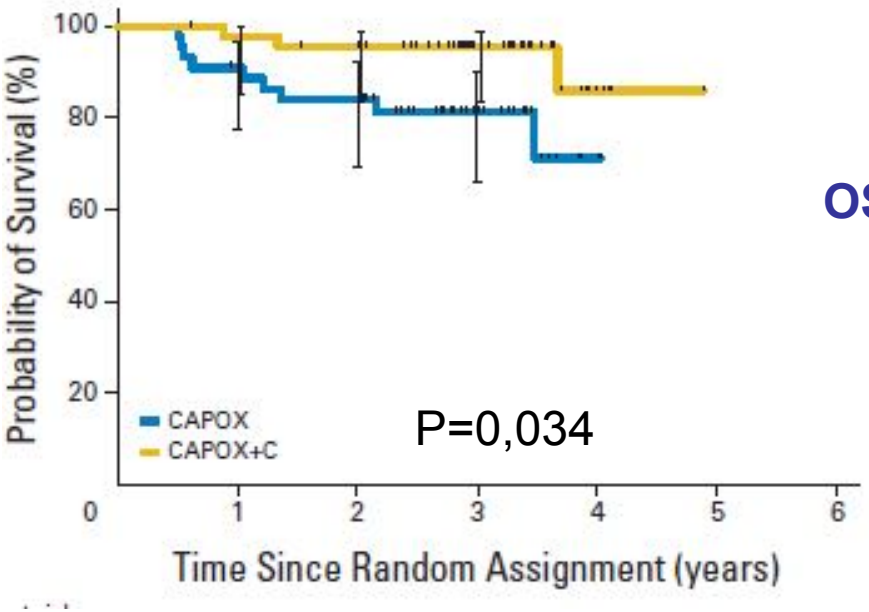
Multicenter Randomized Phase II Clinical Trial Comparing Neoadjuvant Oxaliplatin, Capecitabine, and Preoperative Radiotherapy With or Without Cetuximab Followed by Total Mesorectal Excision in Patients With High-Risk Rectal Cancer (EXPERT-C)



VOLUME 30 · NUMBER 14 · MAY 10 2012

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT



OS in K-ras WT

Conclusion

Cetuximab led to a significant increase in RR and OS in patients with *KRAS/BRAF* wild-type rectal cancer.

Dewdney et al.JCO May 2012

RAS mutations and cetuximab in locally advanced rectal cancer: results of the EXPERT-C trial

Median FUP= 63.8 months

PAN-RAS WILD TYPE *78/149 pts (52%)*	*pCR (%)*	*5y PFS (%)*	*5y OS (%)*
CAPOX	7.5	67.5	70
CAPOX-Cetuximab	15.8	75.5	83.8
	p=0.31	*p=0.20*	*p=0.20*

CONCLUSIONS:

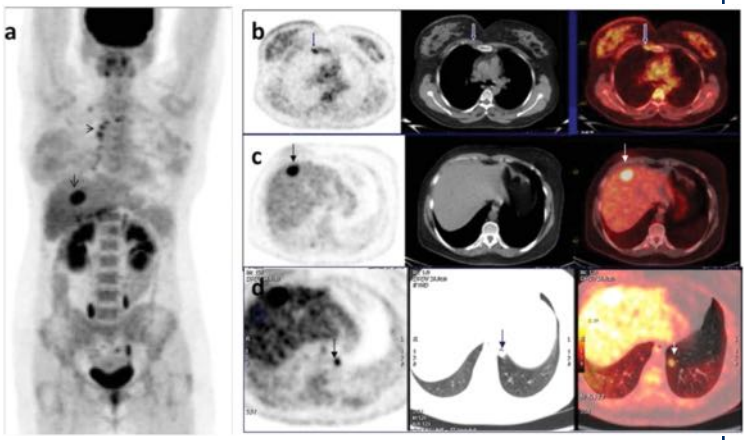
Given the small sample size, no definitive conclusions on the effect of additional RAS mutations on cetuximab treatment in this setting can be drawn and further investigation of RAS in larger studies is warranted.

SCLAFANI, Eur J Cancer. 2014 May;50(8):1430-6

Radiotherapy and new biological molecules: clinical implications

Radiotherapy and targeted therapies

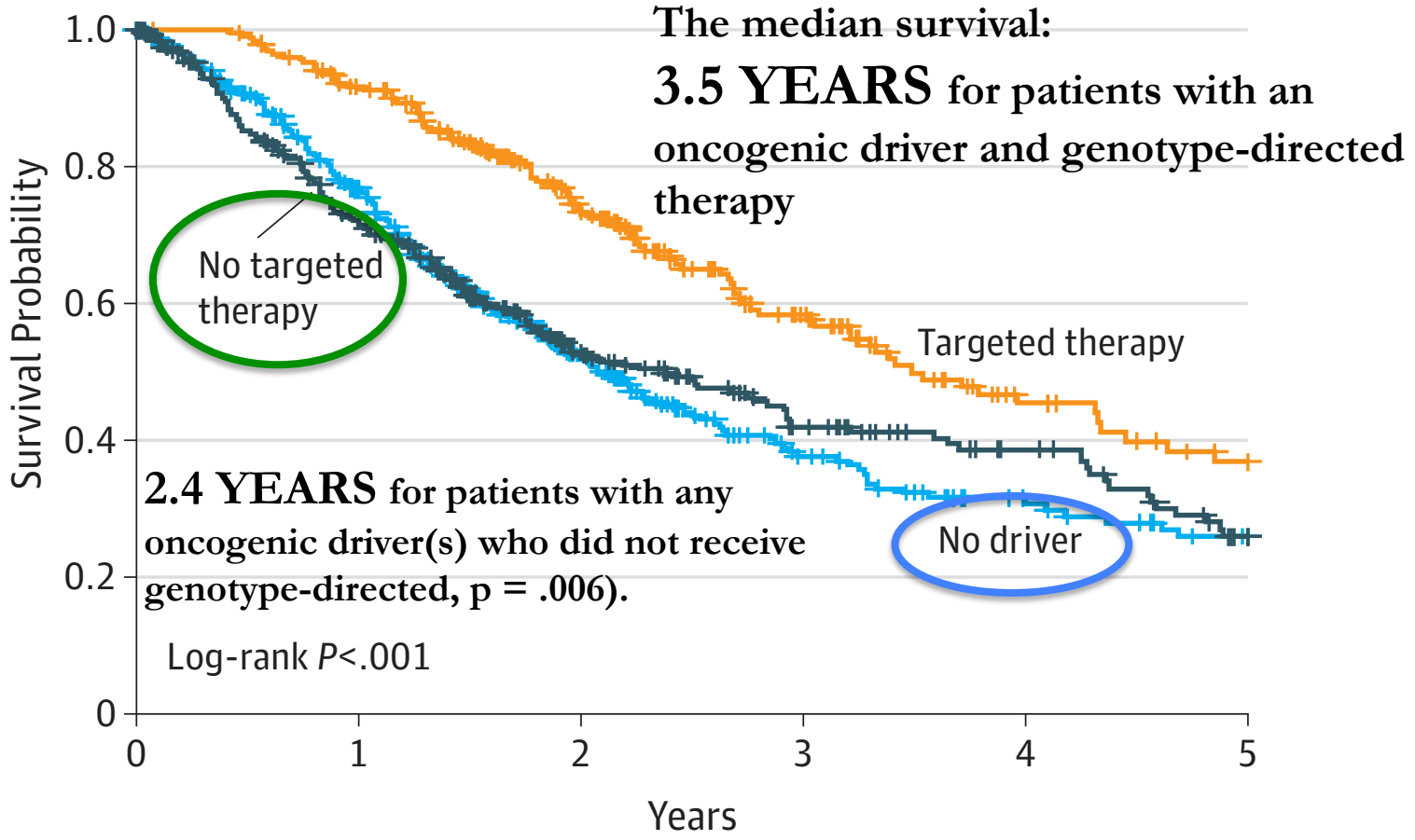
- ✓ Locally advanced disease
- ✓ **Metastatic disease**



Radiotherapy and Immunotherapy

Original Investigation

Using Multiplexed Assays of Oncogenic Drivers in Lung Cancers to Select Targeted Drugs

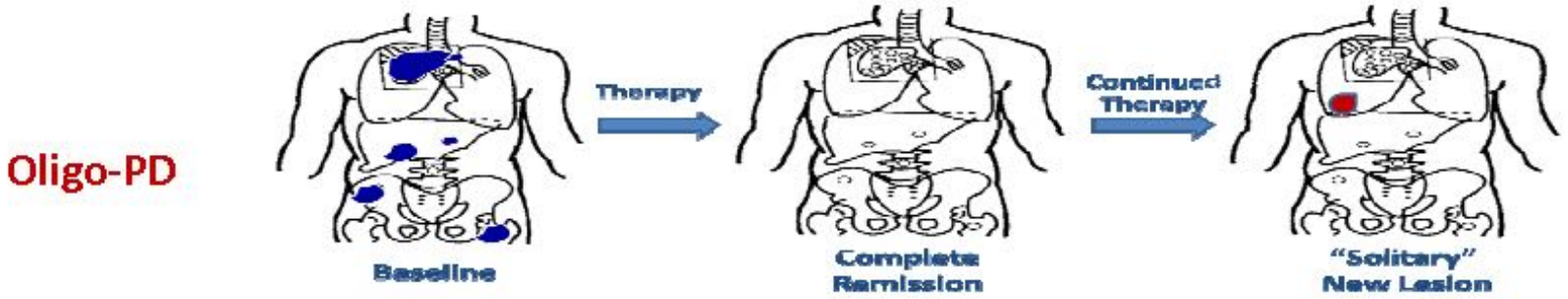


Kris MG, JAMA 2014; 311(19):1998-2006

ESMO Consensus Guidelines: Non-small-cell lung cancer first-line/ second and further lines in advanced disease

For patients who are being treated with EGFR or ALK inhibition and have oligometastatic progression

Recommendation 27: in case of oligometastatic progression during TKI treatment, use a local treatment (such as surgery or radiotherapy) and continue/resume TKI.



Combination of stereotactic ablative body radiation with targeted therapies

Author	Molecular subtype (TKI)	N pts (mutation)	Radiation Dose	PFS after initial TKI (months)	Outcome with SABR
Weickhardt et al. (2012)	EGFR (erlotinib); ALK (crizotinib)	27 (EGFR); 38 (ALK)	15-54 Gy	10.3	6.2 months second PFS after the initial progression on TKI
Gan et al. (2013)	ALK (crizotinib)	38	12-54 Gy	9.1 overall 14 for SABR	5.5 months second PFS after the initial progression on TKI
Yu et al. (2013)	EGFR (erlotinib, gefitinib)	184	45 Gy	12 overall 19 for SABR	10 months second PFS after the initial progression on TKI

In patients with metastatic disease, local control of isolated deposits of resistant subclones might improve clinical outcome.

Zeng J, Lancet Oncol 2014;15:426-34

Is radiation delivery safe if target therapy is concurrently administered?

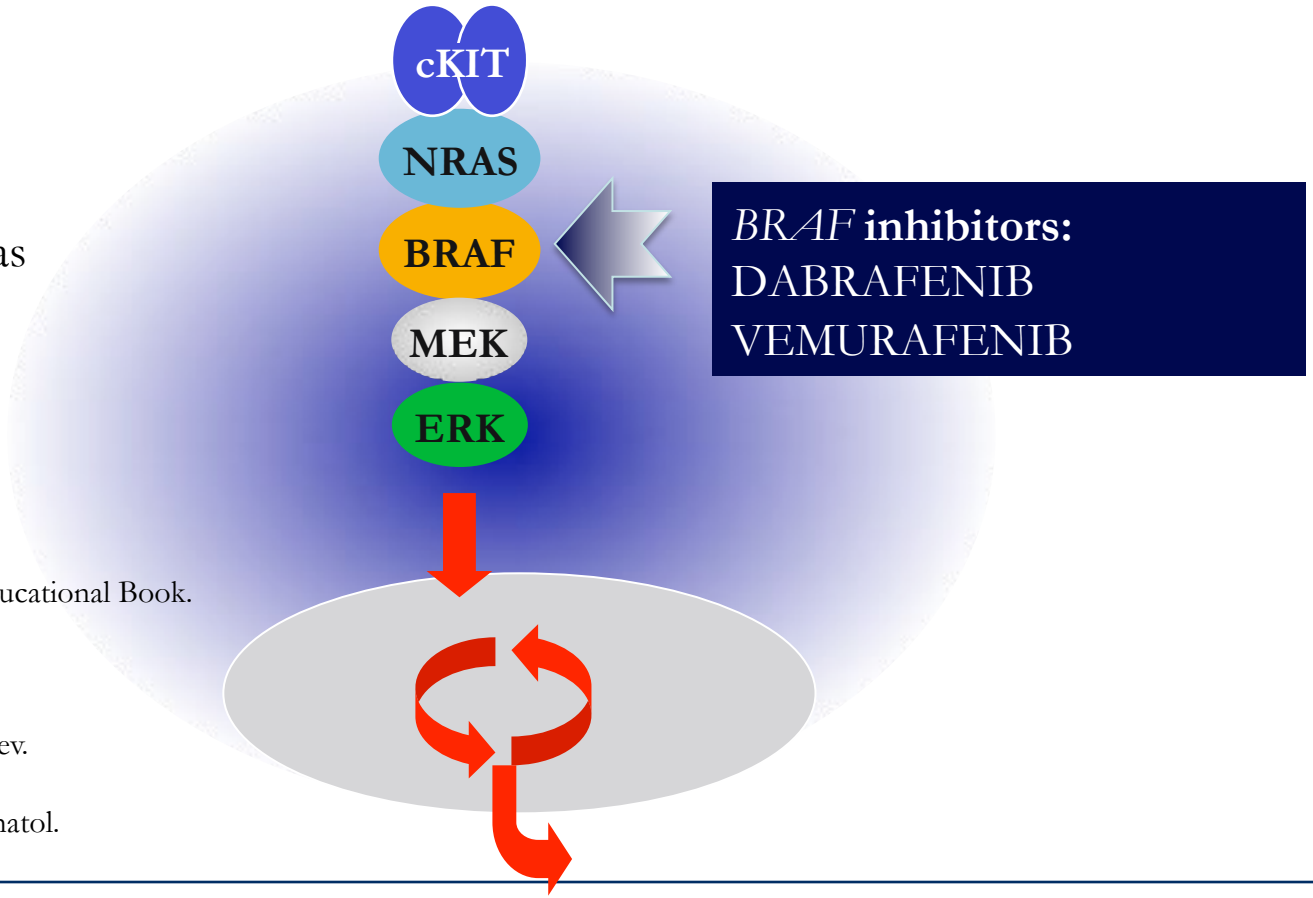
Few clinical data exist on the safety of combination of Radiotherapy with many of the present targeted drugs, and most data are from small patient series with relatively short follow up

The combination of RT and targeted therapies unfortunately might also account for increased toxicity to normal tissue from the combination of the two

MAP Kinase Pathway Targeting in Melanoma

cKIT, NRAS, BRAF mutated in ~ 70% of melanomas, usually mutually exclusive[1]

~42-55% melanomas



***BRAF* inhibitors:**
DABRAFENIB
VEMURAFENIB

Sosman JA, et al. ASCO 2011 Educational Book.
Arkenau HT, et al. Br J Cancer. 2011;104:392-398.
Thomas N, et al. Cancer Epidemiol Biomarkers Prev. 2007;16:991-997.
Nikolaou VA, et al. J Invest Dermatol. 2012;132:854-863.

NOTA INFORMATIVA IMPORTANTE
CONCORDATA CON LE AUTORITA' REGOLATORIE EUROPEE
E L'AGENZIA ITALIANA DEL FARMACO (AIFA)

19 Ottobre 2015

Potenziamento della radiotossicità associata a Zelboraf® (vemurafenib)

Sintesi

- Casi severi di lesioni correlate a radiazioni, alcuni con esito fatale, sono stati riferiti in pazienti sottoposti a radioterapia prima, durante o dopo il trattamento con Zelboraf

- 20 casi di lesioni da radiazioni diagnosticate come recall da radiazioni (n = 8 casi) e sensibilizzazione alle radiazioni (n = 12 casi)

- La maggior parte dei casi è stata di natura cutanea, ma alcuni casi hanno coinvolto gli organi viscerali

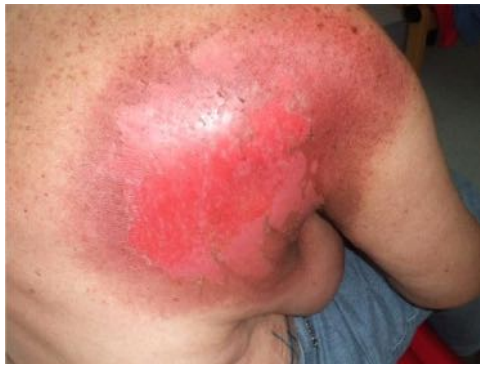
- 8 casi di recall da radiazioni hanno evidenziato un'infiammazione acuta confinata all'area precedentemente irradiata, innescata dalla somministrazione di Zelboraf, 7 o più giorni dopo il completamento della radioterapia.

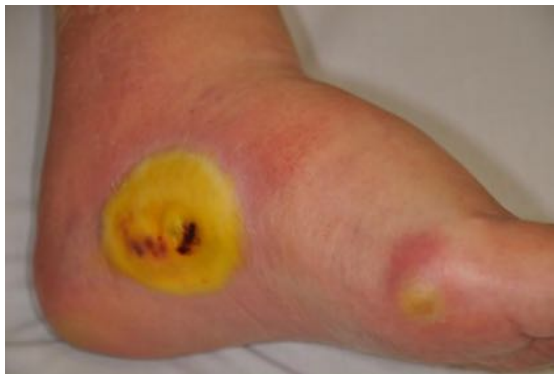
Zelboraf deve essere usato con cautela quando è somministrato prima, in concomitanza o in sequenza al trattamento radiante.

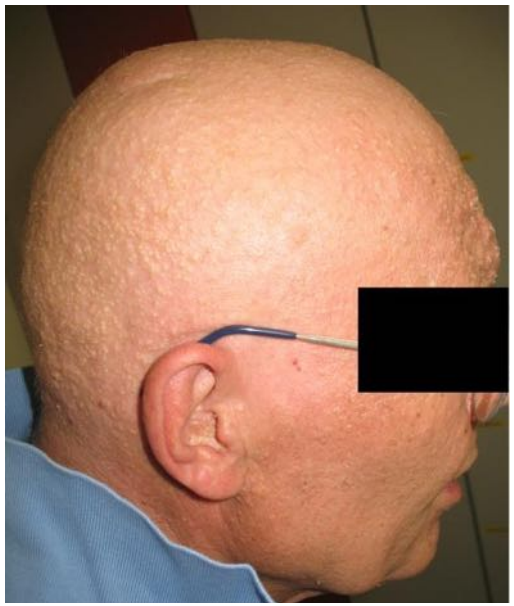
Radiosensitization by BRAF inhibitor therapy – mechanism and frequency of toxicity in melanoma patients

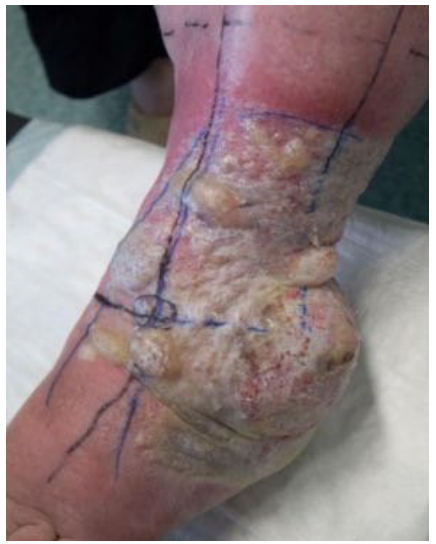
161 melanoma patients were evaluated for acute and late toxicity, of whom 70 consecutive patients received 86 series of radiotherapy with concomitant BRAF inhibitor therapy

43% of acute or late toxicities





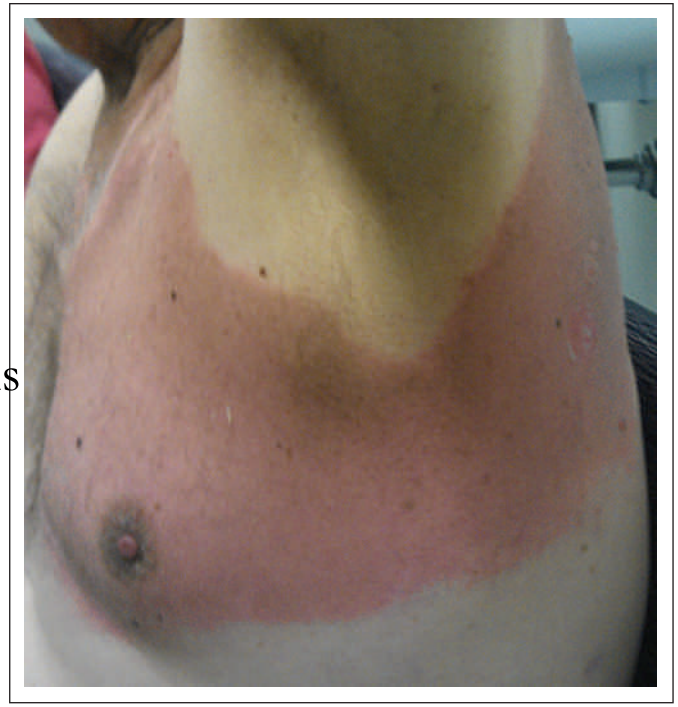




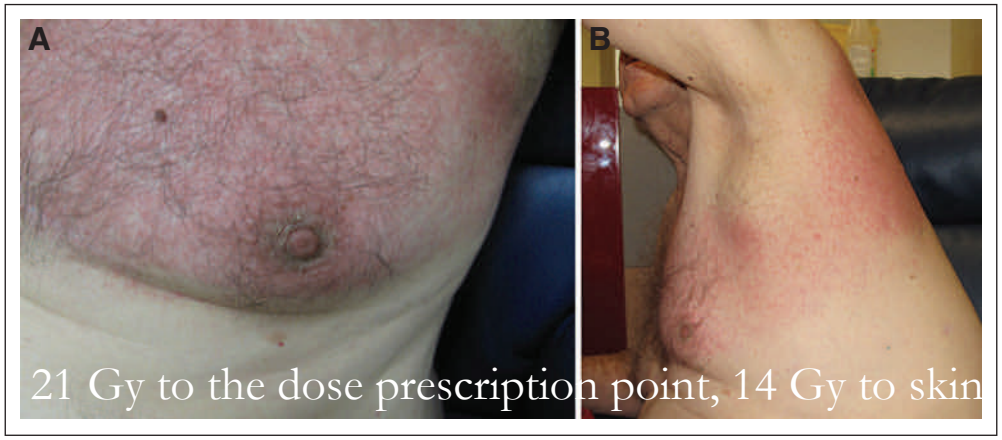
Hecht et al. Annals of Oncology Advance Access published March 11, 2015

ACUTE RADIATION SKIN TOXICITY ASSOCIATED WITH BRAF INHIBITORS

A 71-year-old man with widespread metastatic melanoma
Disease progression in the axilla was treated with palliative radiotherapy of 36 Gy in 12 fractions and Vemurafenib.



27 Gy to the dose prescription point, 18 Gy to skin

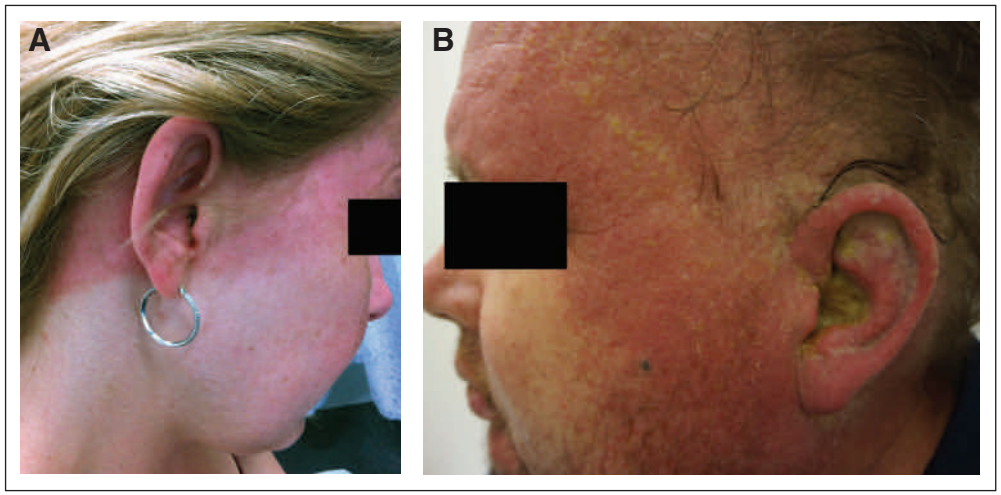


21 Gy to the dose prescription point, 14 Gy to skin

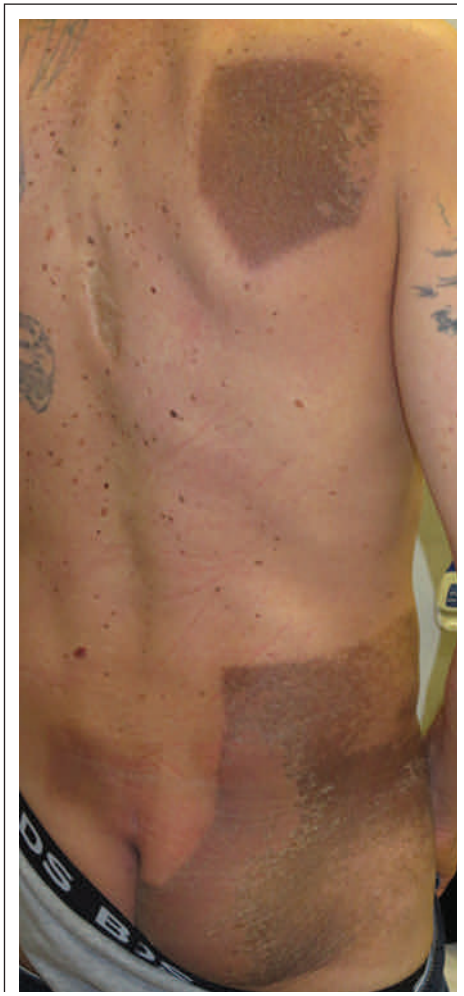
Pulvirenti ,J Clinical Oncol Vol 32, 2014

ACUTE RADIATION SKIN TOXICITY ASSOCIATED WITH BRAF INHIBITORS

RT 8 Gy to painful bony metastases in the left humerus, left ribs, and sacrum.After radiotherapy, he began receiving dabrafenib. He underwent 8 Gy to these new sites of metastatic disease, concurrently with dabrafenib. There was no overlap with his previous radiotherapy fields.



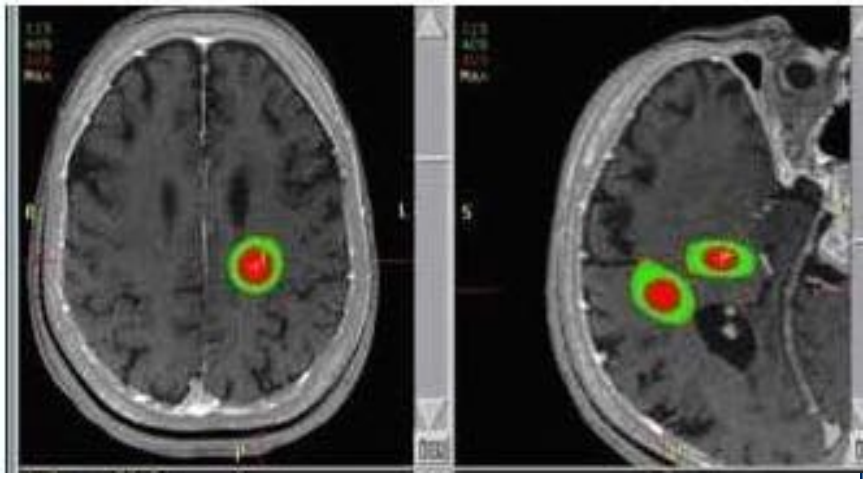
Whole-brain radiotherapy at a dose of 30 Gy in 10 fractions concurrent with dabrafenib

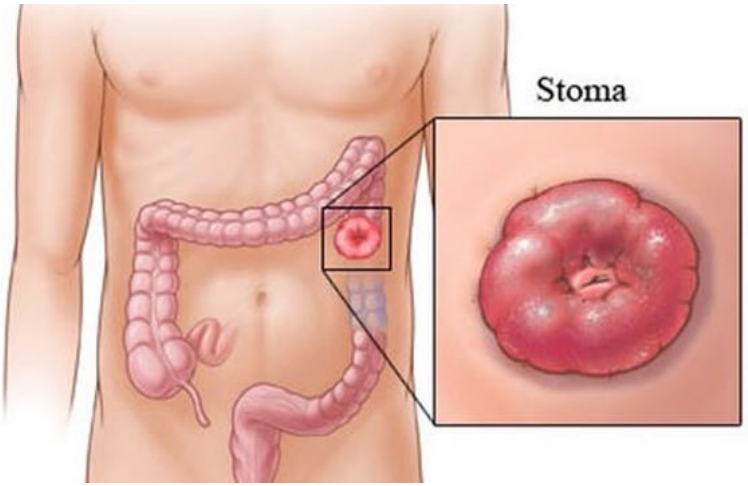


Pulvirenti ,J Clinical Oncol Vol 32, 2014

Severe radiotherapy-induced EXTRACUTANEOUS TOXICITY under vemurafenib.

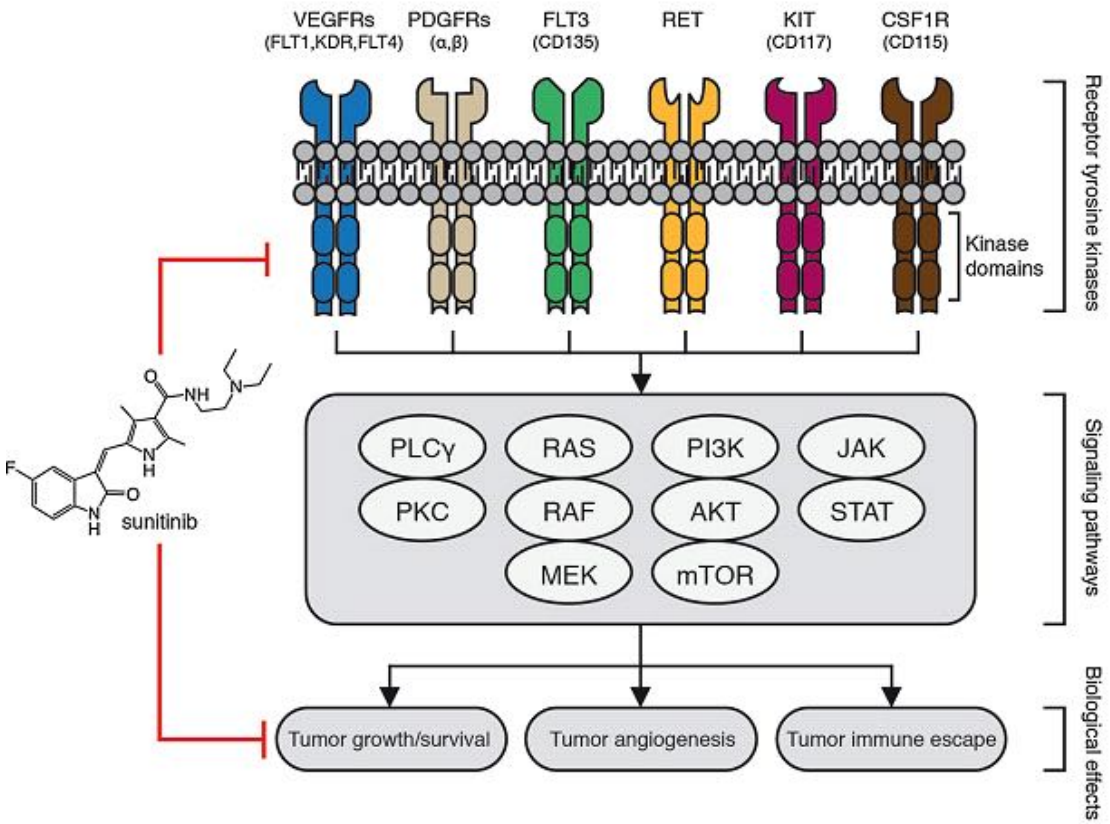
The first patient, a female aged 32, treated with vemurafenib for three months, presented a steroid-dependent RADIONECROSIS after brain stereotactic radiosurgery. Symptoms persisted until her death six months later.

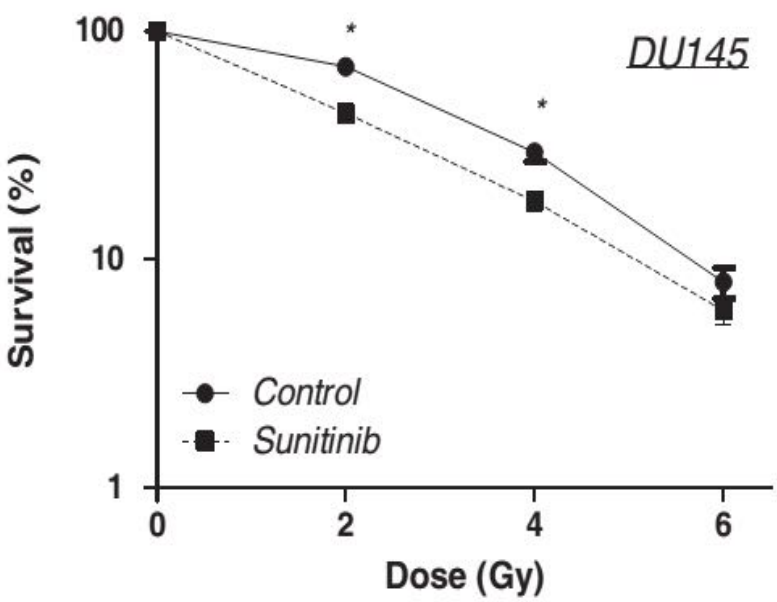




The second patient, a male aged 64 and treated with vemurafenib for nineteen days, presented a radiation-induced ANORECTITIS complicated by diarrhoea, anorexia and weight loss following the concomitant radiation of a primary rectal tumour. A colostomy was needed after ten months in order to improve local status and general health.

Receptor tyrosine kinase inhibitor





Phase II Trial of Concurrent Sunitinib and Image-Guided Radiotherapy for Oligometastases

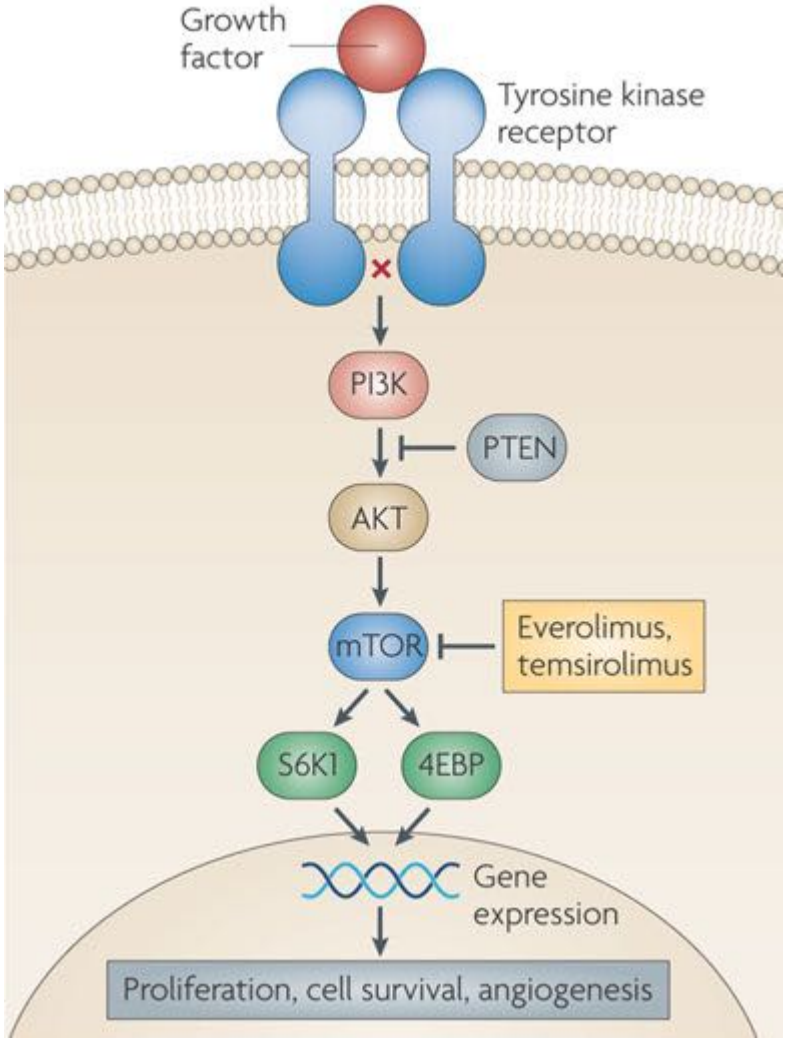
Charles C. L. Tong[1,2], Eric C. Ko[1], Max W. Sung[3], Jamie A. Cesaretti[4], Richard G. Stock[1], Stuart H. Packer[3],

Adverse Event	All grades	Grade 3	Grade 4	Grade 5
Anemia	18	2	0	0
Neutropenia	14	2	0	0
Fatigue	18	0	0	0
LFT abnormalities	15	1	0	0
Thrombocytopenia	15	4	0	0
Mucositis/stomatitis	8	0	0	0
Nausea/vomiting	7	0	0	0
Skin changes	4	0	0	0
Diarrhea	5	0	0	0
Hypertension	3	0	0	0
Bleeding	4	1	0	1*
Metabolic abnormalities	2	1 (PO_4)	0	0
Increased creatinine	5	0	0	0

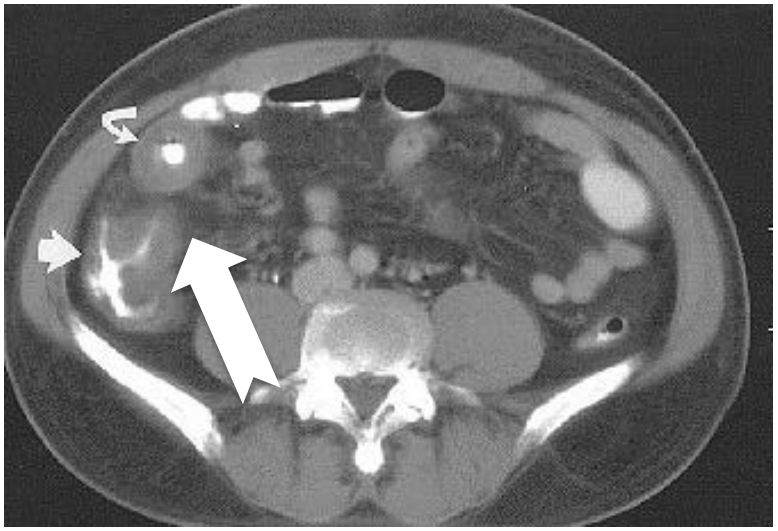
25 patients with oligometastases

Reported a grade 5 gastrointestinal hemorrhage and a fatal bronchobiliary fistula, possibly related to treatment.

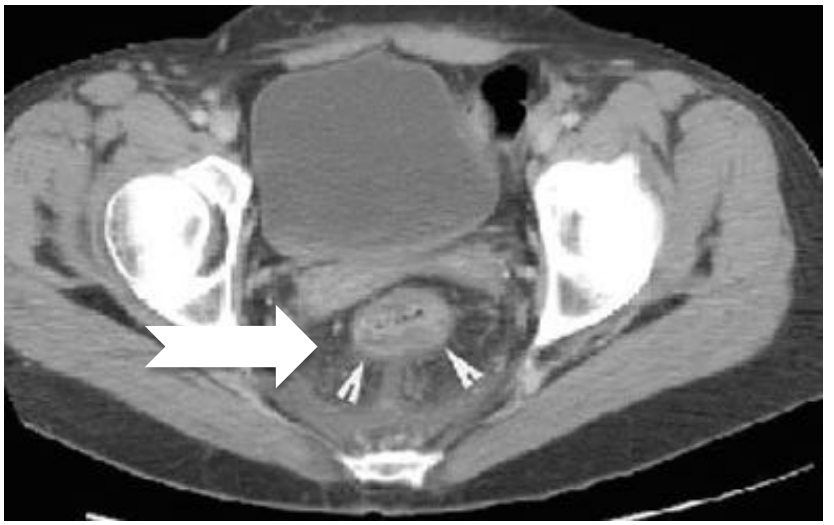
Inhibitor of mammalian target of rapamycin (mTOR)



TOTAL RECALL OF RADIOTHERAPY WITH MTOR INHIBITORS: A NOVEL AND POTENTIALLY FREQUENT SIDE EFFECT?



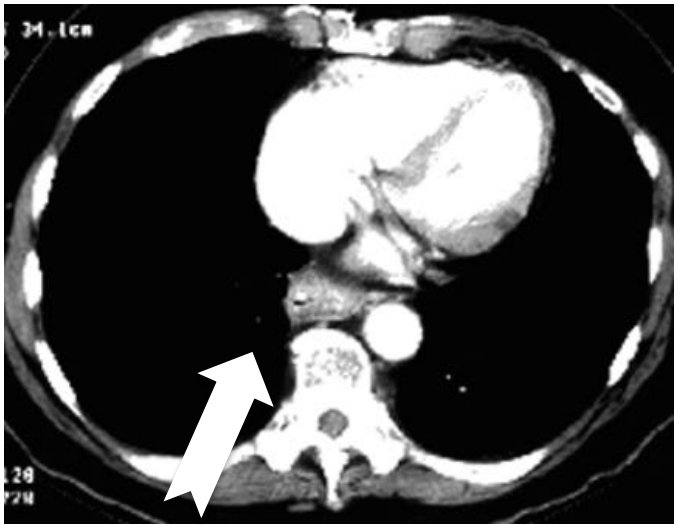
Pelvic RT 2007
4 weeks after the start of temsirolimus (2010), she presented with a subocclusive syndrome associated with grade 2 colitis

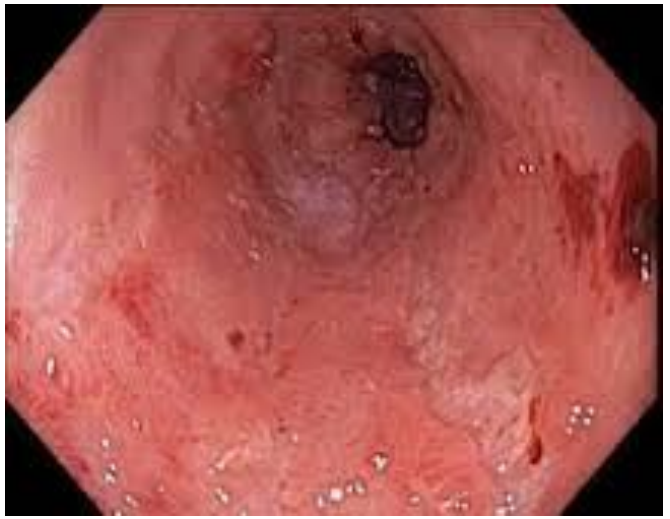


RT for prostate cancer 2006
Temsirolimus for pancreatic cancer 2010

Bourgier C, Ann Oncol 2011

Radiation-Induced Esophagitis exacerbated by Everolimus





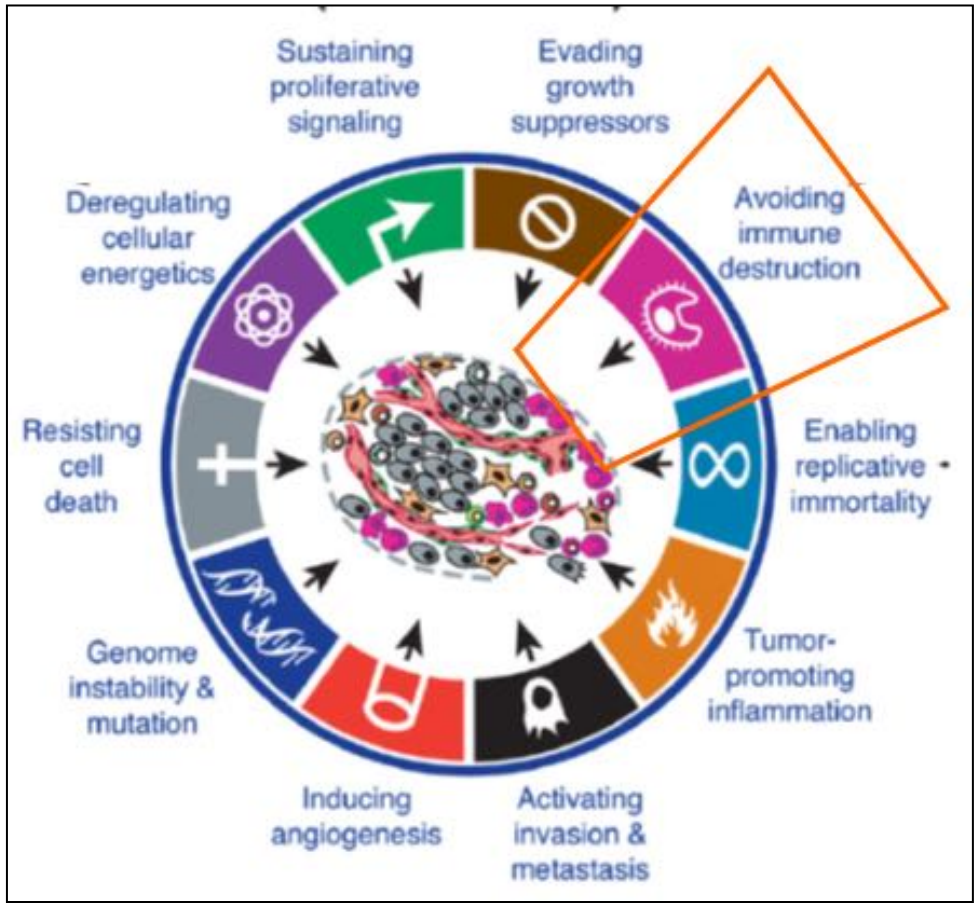
ESOPHAGITIS 3 months after RT:
Breast Cancer Vertebral M+: RT D12 (30Gy/
10 fx)

Attention to possible severe toxicities!!!

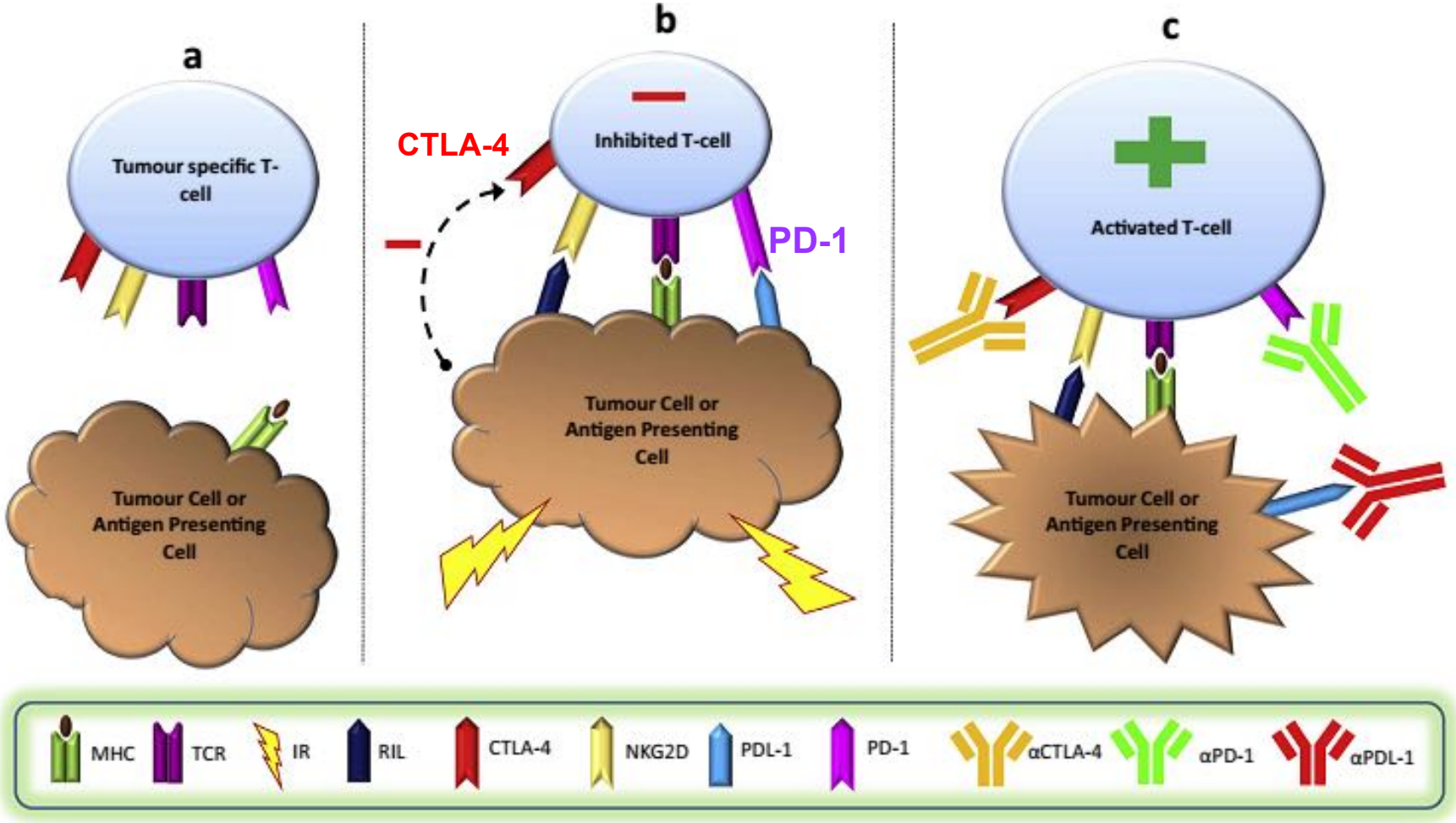
Questions that are important to investigate further

- Timing of RT and target therapy
- Doses of drugs when combined with radiotherapy
- Optimization of fractionating and delivery technique and new dose constraints
- Better patients selections (Anamnesis and collaboration with medical oncologists)

Radiotherapy and Immunotherapy



G.S. Higgins et al./Cancer Treatment Reviews 41 (2015) 105–113

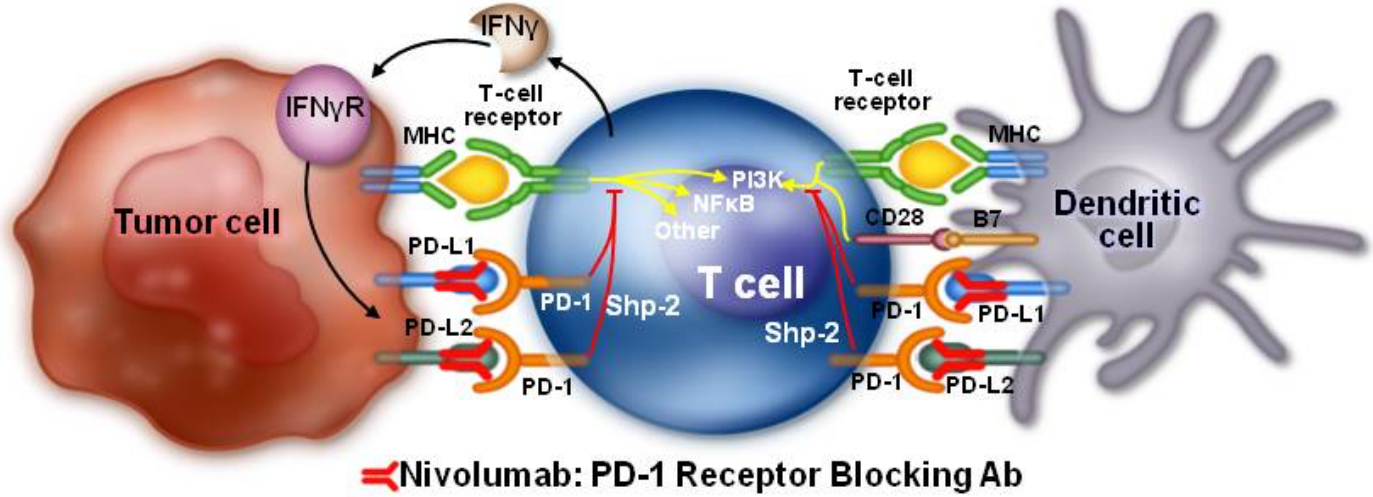


NIVOLUMAB

Presented By David Spigel at 2015 ASCO Annual Meeting

Nivolumab Mechanism of Action

- PD-1 expression on tumor-infiltrating lymphocytes is associated with decreased cytokine production and effector function[11]
- Nivolumab binds PD-1 receptors on T cells and disrupts negative signaling triggered by PD-L1/PD-L2 to restore T-cell antitumor function[12–14]



PRESENTED AT: ASCO Annual '15 Meeting

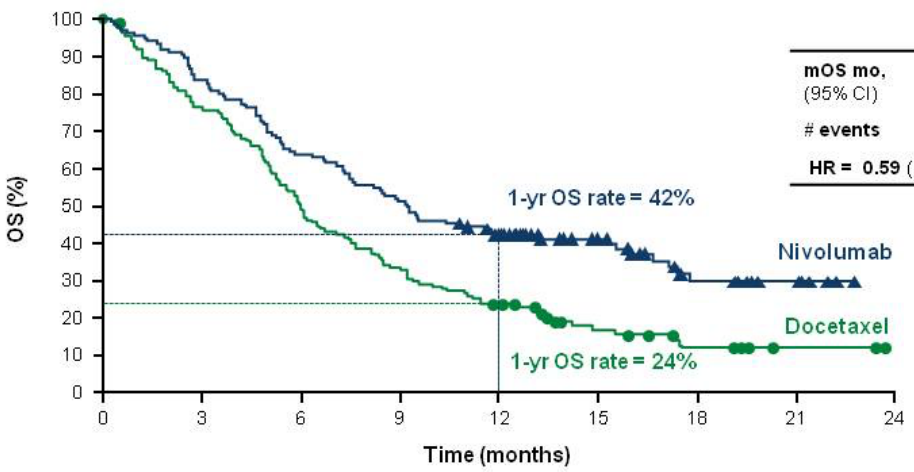
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nivolumab versus Docetaxel in Advanced Squamous-Cell Non–Small-Cell Lung Cancer

Julie Brahmer, M.D., Karen L. Reckamp, M.D., Paul Baas, M.D.,

Overall Survival



	Nivolumab n = 135	Docetaxel n = 137
mOS mo, (95% CI)	9.2 (7.3, 13.3)	6.0 (5.1, 7.3)
# events	86	113

HR = 0.59 (95% CI: 0.44, 0.79), ***P* = 0.00025**

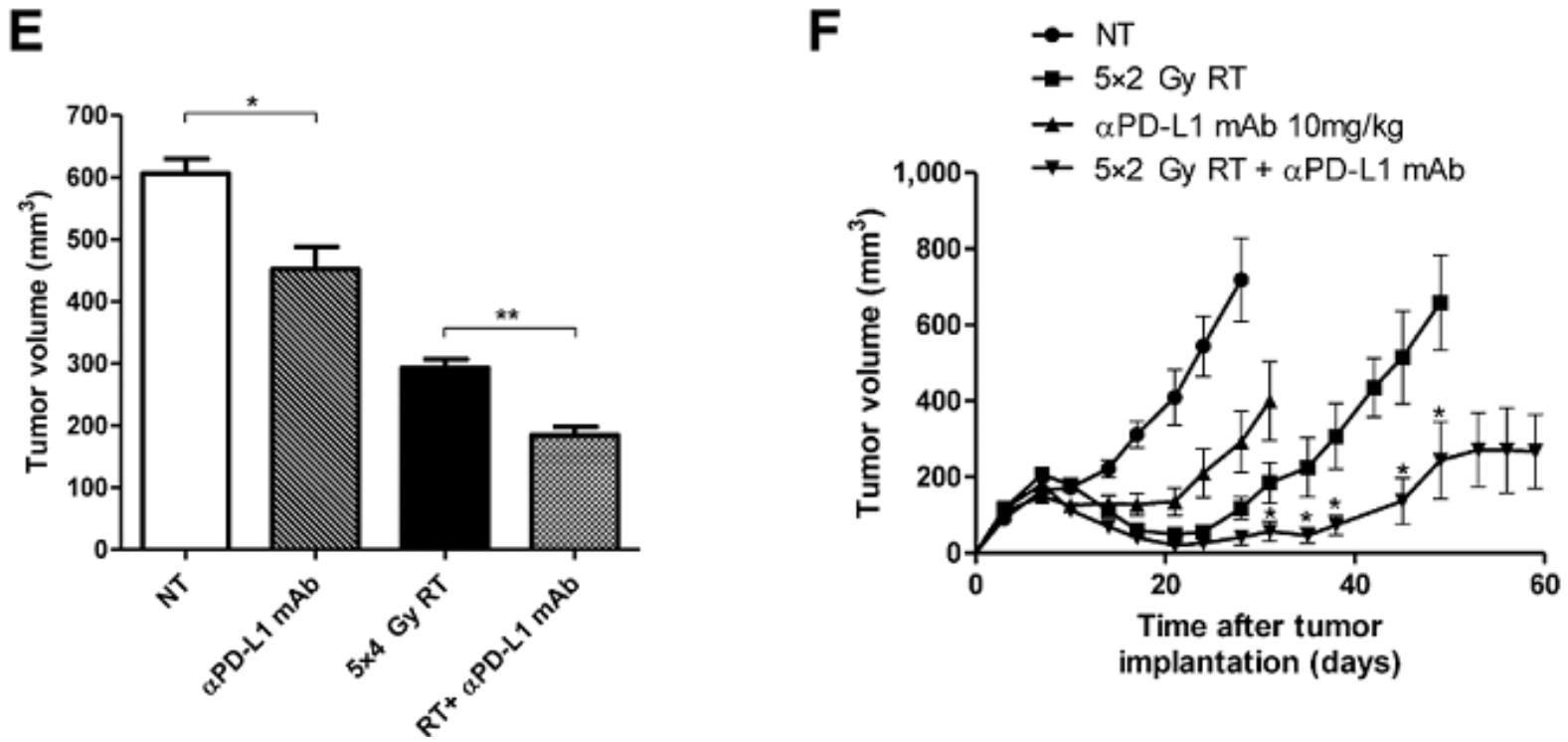
Number of Patients at Risk

Nivolumab	135	113	86	69	52	31	15	7	0
Docetaxel	137	103	68	45	30	14	7	2	0

Symbols represent censored observations

Presented By David Spigel at 2015 ASCO Annual Meeting

Acquired Resistance to Fractionated Radiotherapy Can Be Overcome by Concurrent PD-L1 Blockade



Dovedi et al., Cancer Research; 74 October 2014

Formenti *Journal of Translational Medicine* 2015, **13**(Suppl 1):K10
http://www.translational-medicine.com/content/13/S1/K10

JOURNAL OF TRANSLATIONAL MEDICINE

KEYNOTE SPEAKER PRESENTATION Open Access

Combining radiation therapy with immunotherapy: clinical translation

The novel role of radiotherapy as a powerful adjuvant to immunotherapy warrants more research to define the optimal immunotherapy/RT combinations: currently **35 TRIALS OF RT +IMMUNOTHERAPY** are ongoing in USA.

UNIVERSITA' CAMPUS BIO-MEDICO DI ROMA
www.unicampus.it

Radiotherapy and Immunotherapy

There is a strong biological rationale in exploring feasibility and efficacy of combining radiotherapy and immunotherapy

The diseases (melanoma, lung vs. prostate, breast) and setting (up-front in metastatic disease, oligo-progressive only) where applying this combination remains uncertain …as well as type of RT (optimal dose, SBRT vs standart fractionation)

Conclusions (1)

Improvements in our understanding of tumour and radiation biology have identified multiple new strategies that may enable us to specifically render tumours more sensitive to radiotherapy

Previous trials combining drugs with radiotherapy have failed to live up to expectations due to :

- the lack of reliable predictive biomarkers
- failure to select the most appropriate patients for clinical studies

Conclusions (2)

Novel drugs need to undergo more rigorous pre-clinical testing in order to reduce the risk of producing negative trials and potentially discarding beneficial treatments

If the arsenal of drugs now available to us is used in appropriately selected patients, we may significantly improve clinical outcomes in the future


"Abbiamo una speranza senza fine,
non un fine senza speranza"
(E. Stein)
Grazie!!!