UNIVERSITÀ DEGLI STUDI FIRENZE

aouc

NIVOLUMAB NEL NSCLC SQUAMOSO E NON-SQUAMOSO: L'ESPERIENZA DELLA RADIOTERAPIA ONCOLOGICA DI CAREGGI.

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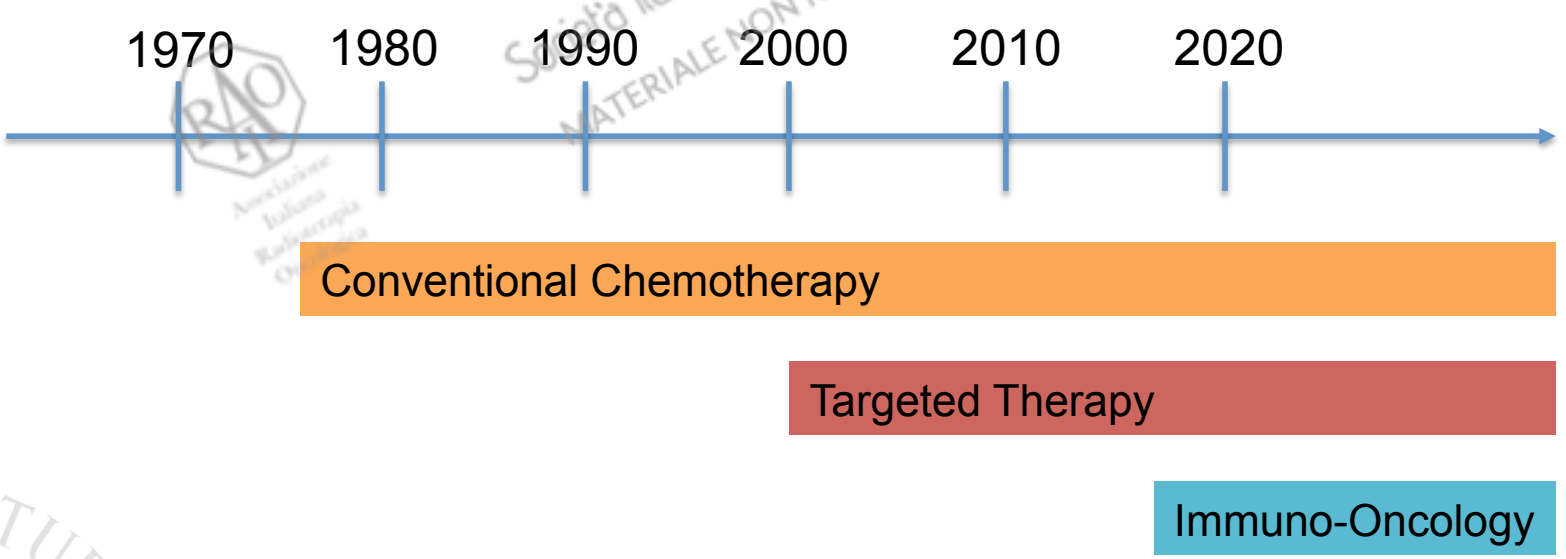
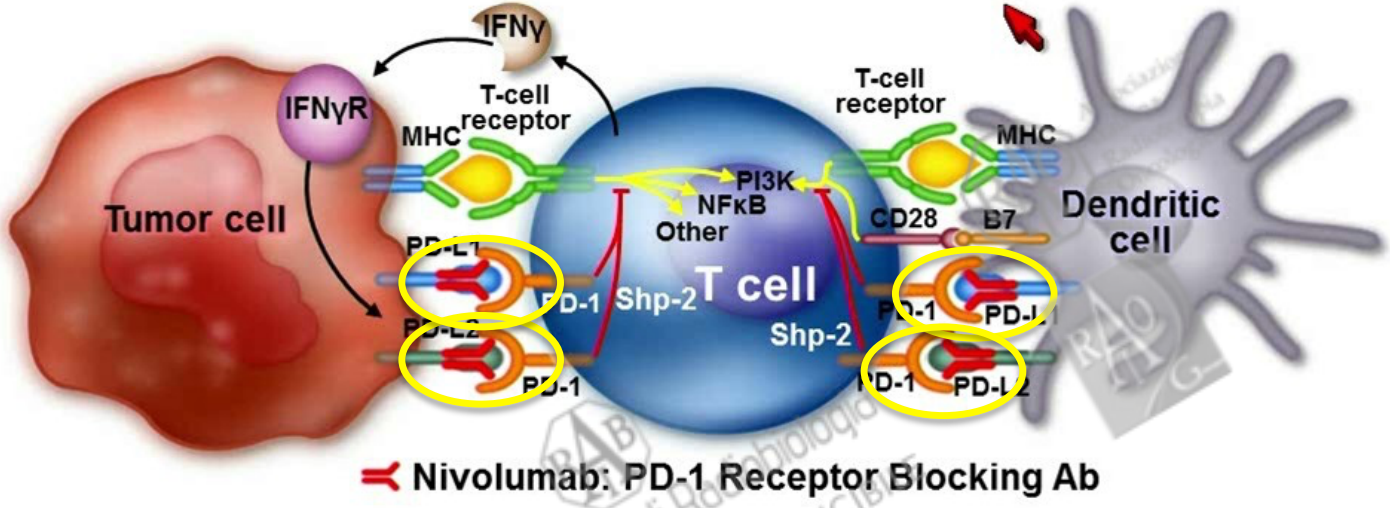
Immuno-Oncology: Storyline

Da dove veniamo? Che siamo? Dove Andiamo? – P. Gauguin (1897)



Immuno-Oncology is the 3° Big Wave in Systemic Therapy for Cancer

Mechanism of Action



Nivolumab binds PD-1 receptors on T cells and disrupts negative signaling triggered by PD-L1/PD-L2 to restore T-cell antitumor function

Milestones

Checkmate 017

Stage IIIb/IV SQ NSCLC
1 prior PT-DC, ECOG PS 0-1
N= 272

Randomize 1:1

Nivolumab
3mg/kg Iv Q2W
N=135
Until PD or unacceptable toxicity

Docetaxel
75 mg/m^2 Iv Q3W
N=137
Until PD or unacceptable toxicity

The median OS was 9.2 months with Nivolumab versus 6.0 months with Docetaxel

Checkmate 057

Stage IIIb/IV NON SQ NSCLC
1 prior PT-DC, ECOG PS 0-1
N= 582

Randomize 1:1

Nivolumab
3mg/kg Iv Q2W
N=292
Until PD or unacceptable toxicity

Docetaxel
75 mg/m^2 Iv Q3W
N=290
Until PD or unacceptable toxicity

The median OS was 12.2 months with Nivolumab versus 9.4 months with Docetaxel

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Demography

		All Treated Patients (N = 24) No.	%
Age			
	Median	66	
	Range	43-81	
Sex			
	Male	12	50
	Female	12	50
Tumor Cell Histology			
	Non Squamous	14	58
	Squamous	10	42
Stage			

Nivolumab Current Status	
Ongoing	12 (50%)
End	12 (50%)

Median Cycles Number: 11,25

Efficacy and Safety of Nivolumab in Elderly Patients With Advanced Squamous NSCLC Participating in the Expanded Access Program in Italy

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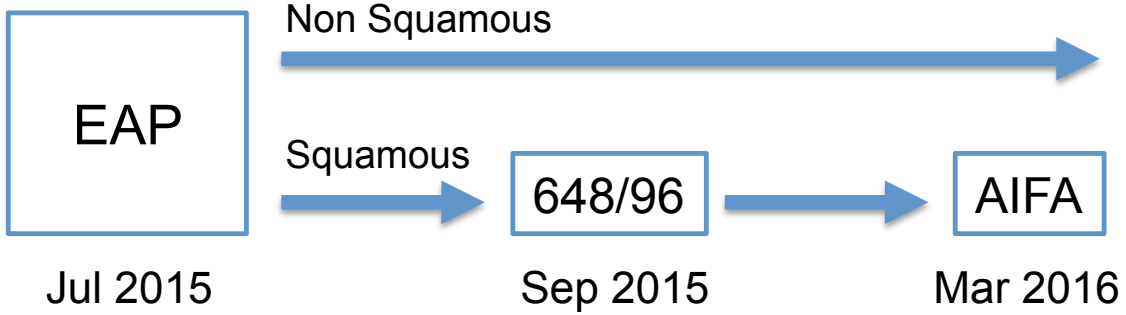
Nivolumab 100 mg/10 ml

3mg/kg Iv Q2W



Toxicity

	GRADE				Total
Sk					7
Mucc					6
Nausea/V					5
Diarr					4
Costip					3
ALT/					3
Fati					3
Dysp					3
Endo					0
Pneur					0
Kidr					0

Remember FIVE

COLITIS
PNEUMONITIS
HEPATITIS
ENDOCRINOPATHIES
SKIN RASH

≤ 10%

Pulmonary	Gastrointestinal	Endocrine
New or Worsening • Shortness of breath • Dyspnea on exertion • Decrease in pulse oximetry • Cough • Wheezing	• Any changes in normal bowel habits • Diarrhea • Blood or mucus in stool • Constipation • Stomach pain/cramps • Nausea • Vomiting • Weight loss	• Headache • Fatigue/weakness • Severe dehydration • Shock • Behavioral changes • Electrolyte disturbances • Hypotension • Heart rate and rhythm abnormalities
Hepatic • *Liver function tests (LFTs) abnormalities, including elevations in AST, ALT, T. Bili* • *Jaundice*	*Skin* • *Pruritus* • *Rash* • *Peeling* • *Skin excoriations*	*Neurological and constitutional* • *Sensory neuropathy* • *Motor neuropathy* • *fever* • *fatigue*

Avera

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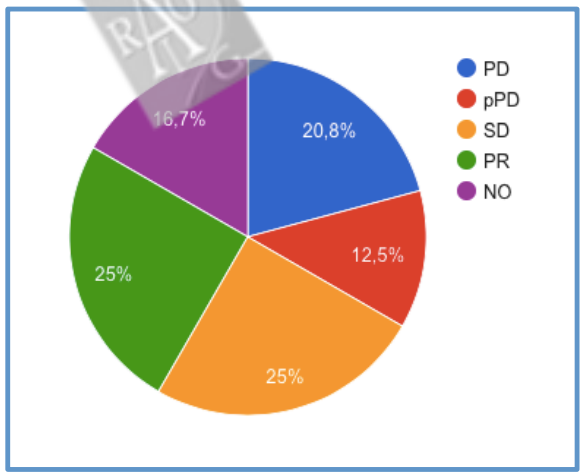
Nausea	12	0	Nausea	34	2
Diarrhea	10	0	Diarrhea	30	2

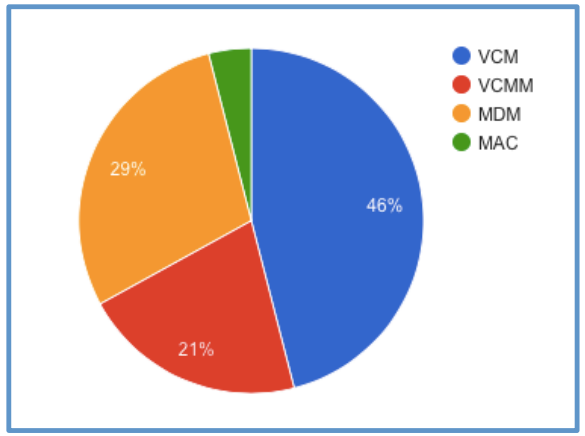
Clinical Outcomes

Time to treatment failure (TTF) is defined as the time from baseline (start of treatment) to discontinuation for any reason, including disease progression, the toxicity of the treatment, the patient's choice or death.

	Days (range)	Months (range)
TTF	180 (26-402)	6 (0.87-13.40)

	N°	Clinical Benefit
CR	0	17/24 patients (71%)
RP	6	
SD	6	
pPD	3	
PD	5	
NO	4	





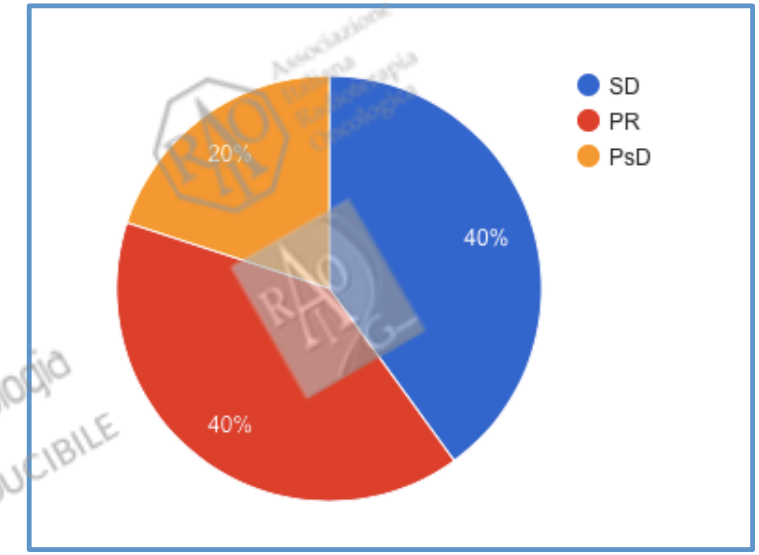
Clinical Outcomes in Fit Patients

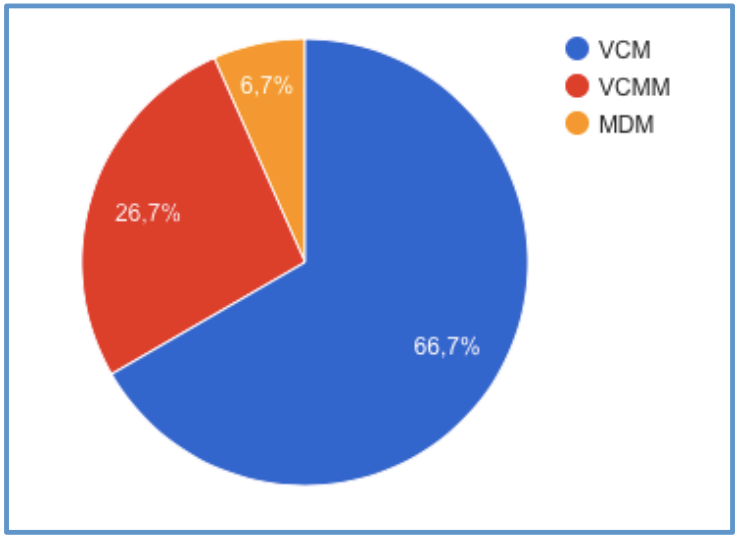
Fit Patients: at least 6 cycles and PS 0-1.

N° of Patients: 15

	Days (range)	Months (range)
TTF	243 (92-402)	8 (3.07-13.40)

	N°	Clinical Benefit
CR	0	12/15 patients (80%)
RP	6	
SD	6	
pPD	3	
PD	0	
NO	0	





Radiation and Dual Checkpoint Blockade Activates Non- Redundant Immune Mechanisms in Cancer

C Twyman-Saint Victor, **AJ. Rech**, **A Maity**, **R Rengan**, **KE. Pauken**, **E Stelekati**, **JL. Benci**, **B Xu**, **H Dada**, **PM. Odorizzi**, **RS. Herati**, **KD. Mansfield**, **D Patsch**, **RK. Amaravadi**, **LM. Schuchter**, **H Ishwaran**, **R Mick**, **DA. Pryma**, **X Xu**, **MD. Feldman**, **TC. Gangadhar**, **SM. Hahn**, **EJ Wherry**, **RH. Vonderheide**, and **AJ. Minn**

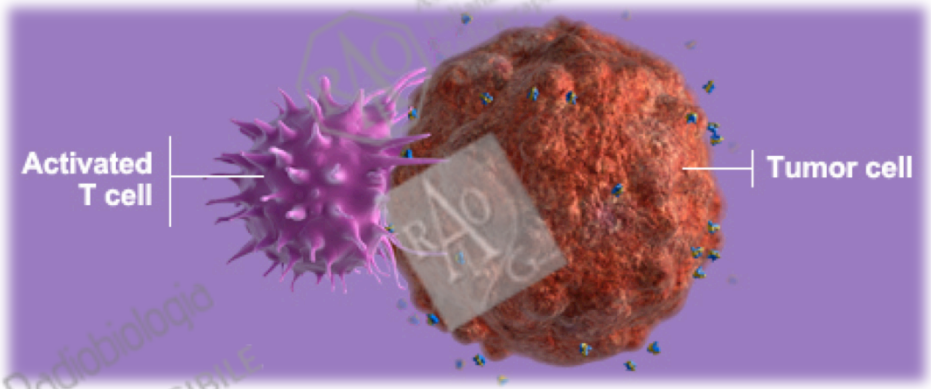
Nature. 2015 April 16; 520(7547): 373–377. doi:10.1038/nature14292.

	Organ	DTF (Gy)	Technique	Stopped Nivolumab (days)	Resumed Nivolumab (days)	Toxicity (grade)
1	Brain	30	WBRT	9	32	Nausea (G1) Fatigue (G1)
2	Kidney	40	SBRT	17	14	-
3	Adrenal	36	SBRT	22	24	Fatigue (G1)
4	Brain	30	SBRT	14	38	-

Conclusions

NIVOLUMAB MONOTHERAPY
3 mg/kg IV q2w

- Well tolerated
- Good responde profile
- Encouraging data on survival



Radiotherapy during treatment doesn't show an increased toxicity.

It will be necessary to continue the analysis to obtain more information about survival and response rate.

Thanks for Your Attention