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Farmaci innovativi
e ipofrazionamento

PALACONGRESSI DI RIMINI
30 settembre, 1-2 ottobre 2016

Pemetrexed e radiochirurgia con gammaknife in pazienti con metastasi cerebrali da adenocarcinoma polmonare: l'esperienza di un singolo centro

R. Grassi, D. Greto, S. Scoccianti, I. Desideri, B. Detti, L. Poggesi, G. Francolini, L. Bordi, P. Bono, M. Loi, G. Simontacchi, P. Bonomo, L. Livi

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Background

NSCLC Adenocarcinoma → BRAIN METASTASES (BM) occur in 30-50%

- THERAPEUTIC STRATEGIES -

(Non-Squamous cell carcinoma, **NO** ALK/EGFR mutation)

❖ **SURGERY**

❖ **CHEMOTHERAPY → CDDP+/ Pemetrexed /Gemcitabine/ Vinorelbine/ Taxani**

❖ **WBRT**

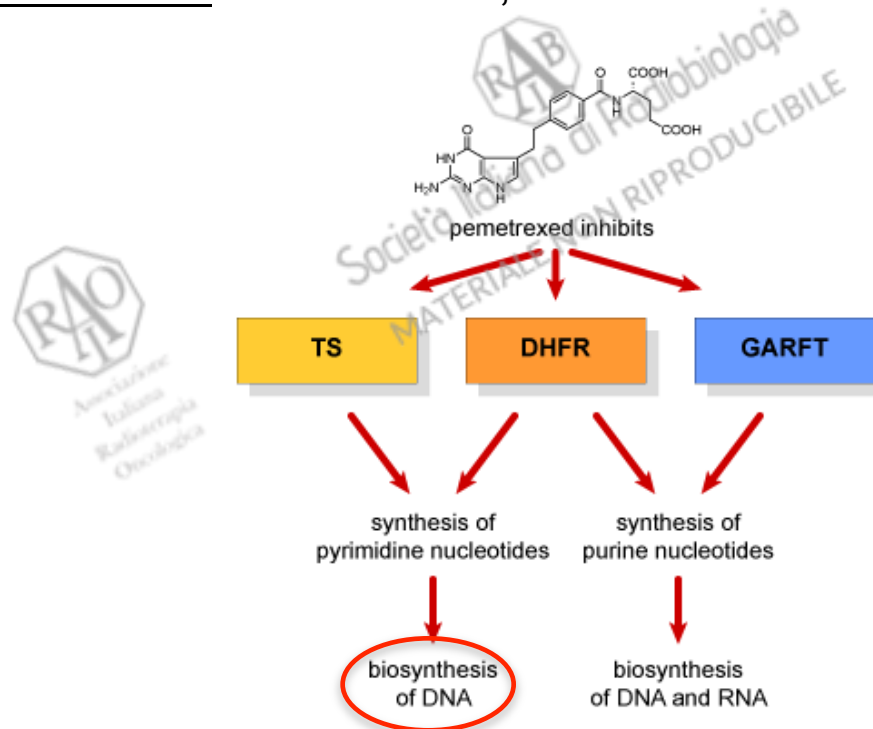
❖ **SRS**



Pemetrexed

Antifolate Multitarget:

- Inhibition of several enzymes in the folate pathway → decrease thymidine
- Need of premedication with folic acid, vitamin B12 and corticosteroids



✓ 500 mg/m² in monotherapy or in association with cisplatin



Pemetrexed

VOLUME 26 • NUMBER 21 • JULY 20 2008

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

First line

In Metastatic NSCLC
with BM

Phase III Study Comparing Cisplatin Plus Gemcitabine
Cisplatin Plus Pemetrexed in Chemotherapy-Naive
With Advanced-Stage Non-Small-Cell Lung Cancer

Agliotti, Purvish Parikh, Joachim von Pawel, Bonne Biesma, Johan Vansteenkiste,
Christian Manegold, Piotr Serwatowski, Ulrich Gatzemeier, Raghunadharao Digumarti, Mauro Zukin,

Ann Oncol. 2011 Nov;22(11):2466-70. doi: 10.1093/annonc/mdr003. Epub 2011 Feb 14.

Pemetrexed and cisplatin as first-line chemotherapy for advanced non-small-cell lung cancer (NSCLC) with asymptomatic inoperable brain metastases: a multicenter phase II trial (GFPC 07-01).

Barlesi F¹, Gervais R, Lena H, Hureauux J, Berard H, Paillot D, Bota S, Monnet I, Chajara A, Robinet G.

Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): a double-blind, phase 3, randomised controlled trial.

Paz-Ares L¹, de Marinis F, Dediu M, Thomas M, Pujol JL, Bidoli P, Molinier O, Sahoo TP, Laack E, Reck M, Corral J, Melemed S, John W, Chouaki N, Zimmermann AH, Visseren-Grul C, Gridelli C.

Pemetrexed + Cisplatin → prolonged survival

Radiosurgery



National
Comprehensive
Cancer
Network®

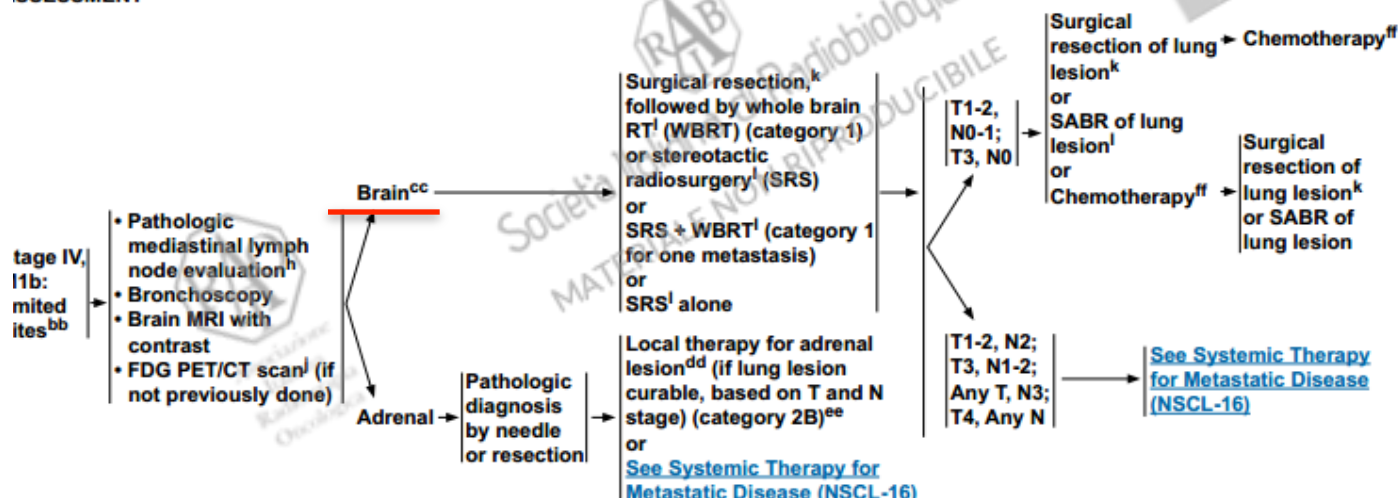
NCCN Guidelines Version 4.2016 Non-Small Cell Lung Cancer

[NCCN Guidelines Index](#)
[NSCLC Table of Contents](#)
[Discussion](#)

CLINICAL ASSESSMENT

PRETREATMENT EVALUATION

INITIAL TREATMENT



Indications: Limited lesions size and number and controlled extracranial disease



Aim

In patients with Brain metastases and primary NSCLC
Treated with the combination of
PEMETREXED and **SRS**

Report:

- **Safety**



- **Clinical outcome**

LPFS*

OS

DBPFS*

*LPFS: local progression free survival

*DBPFS: distant brain progression free survival



Materials and Methods

Retrospective analysis

- From **June 2013** to **December 2015**
- **16 Patients** advanced NSCLC with BM

• **INCLUSION CRITERIA:**

- 1. Primitive and extracranial disease controlled
- 2. MRI performed within 20 days before RSR
- 3. Adequate bone reserve
- 4. Good hepatic and renal function

Local relapse → radiological evidence of progression treated BM

Distant brain progression → development new metastases



Materials and Methods

- **PEMETREXED:** Pemetrexed → as I or further line chemotherapy

500 mg/m², administered intravenously on day 1, every 21 days
(All the patients received premedication with vitamin B12, folic acid and corticosteroid)

- **RADIOSURGERY:** All patients treated with Gammaknife Perfexion

ONLY local treatment

Int J Radiat Oncol Biol Phys. 2000 May 1;47(2):291-8.

Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05.

Shaw E¹, Scott C, Souhami L, Dinapoli R, Kline R, Loeffler J, Farnan N.





Results

Patients characteristics

AGE			GENDER		KPS		RPA		GPA		
<60	60-70	>70	M	F	<70	≥70	1	2	0-1	1,5-2,0	2,5-3
31.5%	43.7%	24.8%	75 %	25%	0%	100%	37,5%	62,5%	18,7%	37,5%	43,8%

Prior WBRT		BM at DIAGNOSIS	
Y	N	3	≤ 2
25%	75%	26%	47,3%

*100% patients has extracranial metastases and primary tumor CONTROLLED

Results

Treatments caratheristic

BM treated		NEW BM at MRI		Pemetrexed		Dose (Gy)	
≤3	≥4	Y	N	CDDP associated	Maintenance	<20	>20
43,75%	56,2%	68,7%	31,3%	75%	25%	14%	86%

PEMETREXED: Mean number of cycles at SRS → 5

Median interval beetwen chemo-administration and SRS: 20 days

1 patient had planned chemotherapy interruption for 1 cycle

RSR: Mean dose → 22 (range 15 – 24 Gy)

Mean BM treated → 4 (range 1-8)



Results

FOLLOW UP was performed:

- Clinical evaluation
- MRI @ 1 month
- MRI @ 3 months
and every 3 months thereafter

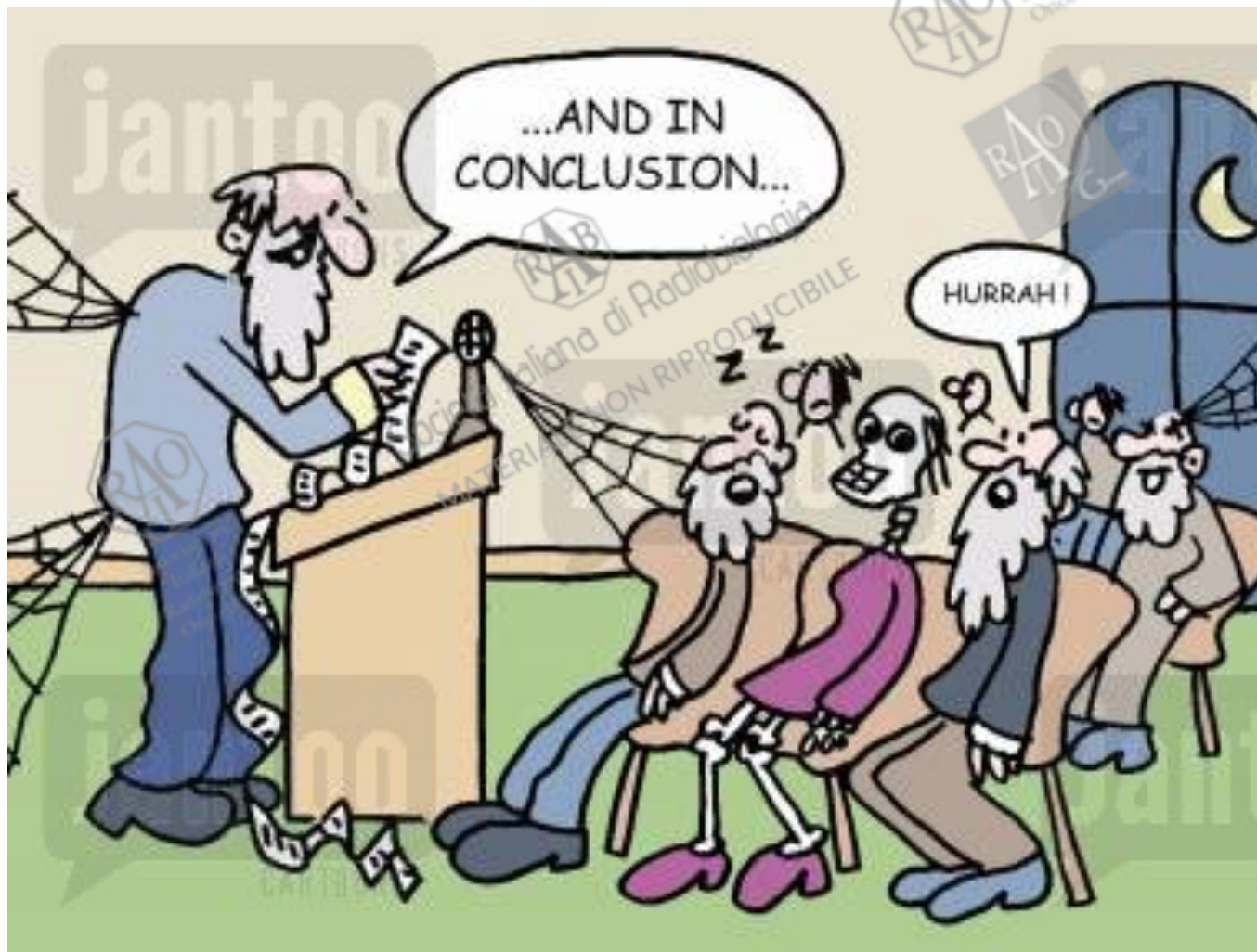
Safety

~~NEW neurologic symptom~~
~~Chemotherapy interruptions due to toxicity~~
~~Signs of Radionecrosis~~

OUTCOMES at 12 months	LDPFS	DBPFS	OS
	71,5%	31,2%	64,2%

43,7% patients were deceased, 1 pt for neurological causes, 6 for PD

Conclusion





Conclusion

SRS associated to Pemetrexed is a **safe treatment combination** for BM adenocarcinoma patients.

Not
compromising clinical
outcome

Delaying chemotherapy
change

Continuation
therapy
with Pemetrexed

**THANK YOU FOR YOUR
ATTENTION**

**NO QUESTIONS,
PLEASE**



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MATERIALE NON RIPRODUCIBILE

