

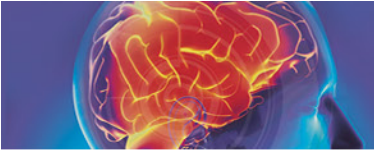
# 9<sup>th</sup> Annual Brain Metastases Research and Emerging Therapy Conference

**October 4-5, 2019  
Marseille, France**

# Combined Immunotherapy And Radiation therapy

## CON

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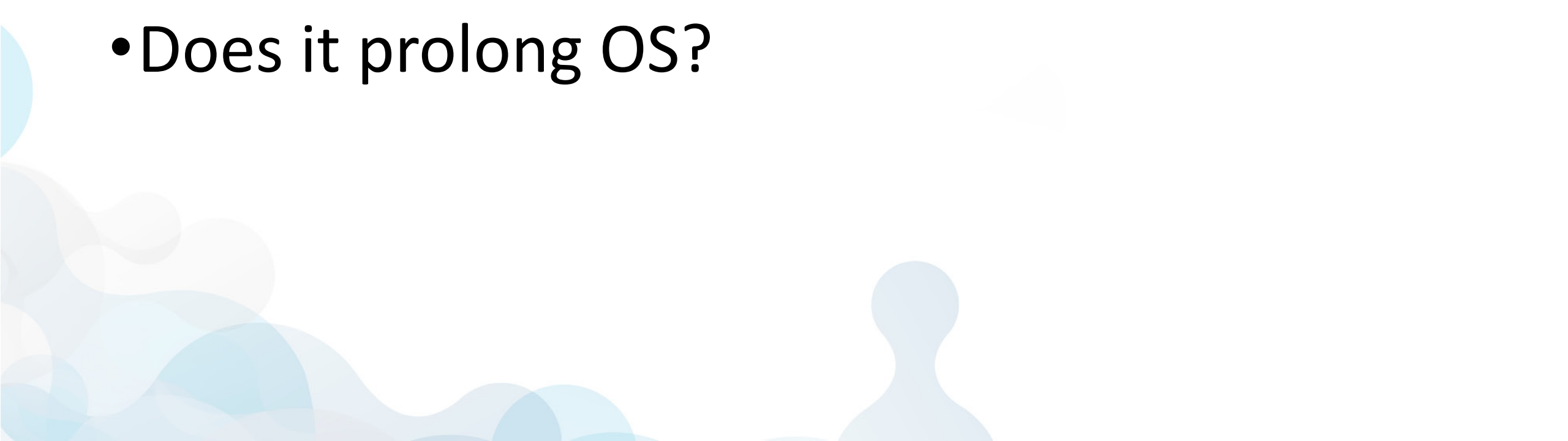


# What is „combined“ RT and immunotherapy?

- There is no consensus on the duration of delay between RT and CIT
- Is it:
  - Within 1 year?
  - Within 6 months?
  - Within 4 months?
  - Within 3 months?
  - Within 1 month?
  - Within 30 days?
  - Within 4 weeks?
  - +/- 3 days?
  - 1 day?



# Combining immunotherapy and radiation therapy

- Is it safe?
  - Does it prolong PFS?
  - Does it prolong OS?
- 



# Safety

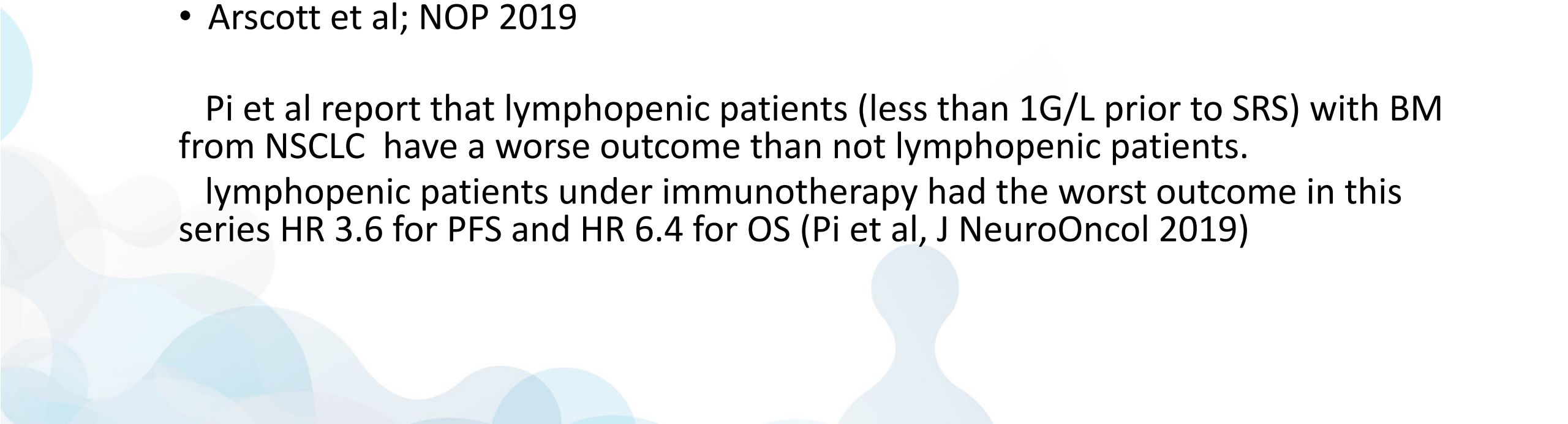
- **Acute side effects:**

No difference to either immunotherapy alone or SRS alone observed

- Shepard et al, J Neurosurg 2019
- Chen et al, Int J Rad Oncol Biol Phys 2017
- Pike et al, Radiother Oncol 2017
- Arscott et al; NOP 2019

Pi et al report that lymphopenic patients (less than 1G/L prior to SRS) with BM from NSCLC have a worse outcome than not lymphopenic patients.

lymphopenic patients under immunotherapy had the worst outcome in this series HR 3.6 for PFS and HR 6.4 for OS (Pi et al, J NeuroOncol 2019)



# Safety

- **Long term:** more radionecrosis?

Pires da Silva et al, doi: 10.1111/pcmr.12775

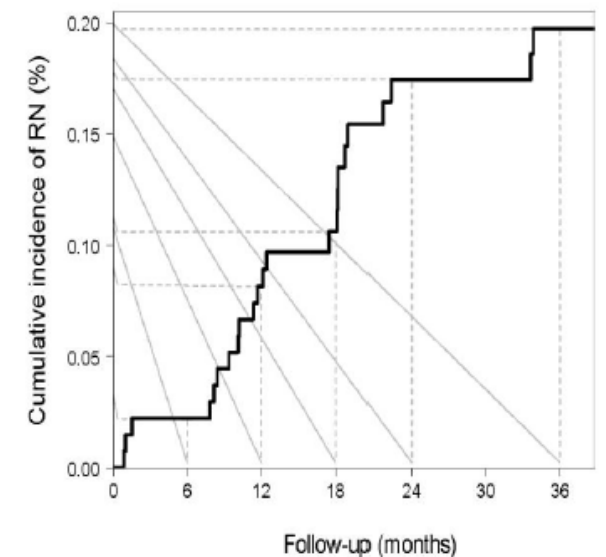
Retrospective analysis of radionecrosis in 12 academic centres

Patients with BM from MM treated with anti-PD-1 +  
WBRT or SRS, surviving at least 1 year after RT

Radionecrosis occurred in 2% , 8%, 11%, 18%

at 6 12 18 24 months

Figure 1. Cumulative incidence of radionecrosis

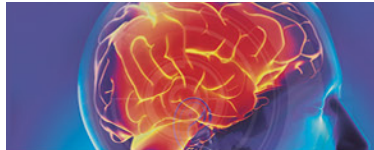


## Risk factors for radionecrosis

LABEL	Univariable Analysis		Multivariable Analysis	
	OR	P-value	OR	P-value
<b>LDH<sup>a</sup> level</b>		<b>0.0151</b>		<b>0.0496</b>
Normal	1		1	
Elevated	2.61 (1.20, 5.66)		2.33 (1.00, 5.44)	
<b>M-staging<sup>b</sup></b>		0.0717		0.6345
Other	1		1	
M1c	2.17 (0.93, 5.04)		1.26 (0.49, 3.22)	
<b>Prior ipilimumab</b>		<b>0.0142</b>		<b>0.0319</b>
No	1		1	
Yes	3.11 (1.26, 7.69)		2.79 (1.09, 7.10)	

## Current experience on sequence of treatments for RT and Checkpoint Inhibitor Therapy ( CIT) in brain mets

Author	Study design	Patients n	tumor	CIT	PFS			OS		
					RT>CIT	Combined	CIT>RT	RT>CIT	Combined	CIT>RT
Patel, 2017	P	54	MBM	Ipi	-	-	-	-	37% at 1year	-
Chen, 2015	R	74	MBM, NSCLC	IPI, NIV	-	-	-	-	better	-
Sik, 2013	R	33	MBM	Ipi	-	-	-	19.9	-	4.0
Skrepnik, 2017	R	25	MBM	Ipi	>50	30	4.2	Not reached	Not reached	Not reached
Kiess, 2015	R	113	MBM	Ipi	-	-	-	66% at 1 year	65%	40%
Cohen-Inbar, 2017	R	46	MBM	Ipi	5.0	7.2	7.2	6.4	13.8	13.8
Rahman, 2017	R	82	MBM	Ipi, Pem	-	-	-	-	better	-
Quian, 2016	R	75	MBM	Ipi, Pem	-	-	-	-	19.1	-



# Conclusions

- So far mainly retrospective data
- Nearly exclusive on melanoma brain mets
  
- **TOO EARLY FOR CONCLUSIONS!**
- Prospective data necessary to answer this question:
- ongoing study from Melanoma Institute Australia





**VOTRE TEXTE**

