

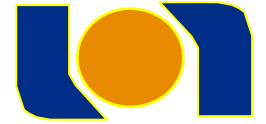


# **The abscopal effect: Efficacy of Radiotherapy in patients on progression after treatment with ipilimumab 3 mg/kg.**

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# **What does it mean Abscopal ?**

***From Latin *ab* ("away from") and Ancient  
Greek σκοπός (*skopos*, "target, aim")***



# Abscopal Effect

## **Abscopal Effect:**

“a rare phenomenon where locoregional irradiation of a tumor causes, not only a shrinking of the irradiated tumor, but also a shrinking of tumor lesions far from the irradiated area”.

# Background



Evidence suggests that the combination of radiation and immunotherapy can prevent cancer cells from evading an immune response via several mechanisms

The synergistic effect of RT plus immunotherapy may explain the abscopal effect, whereby radiation can inhibit distant tumours after localised therapy

Only a small number of early phase trials have investigated the combination of RT and immunotherapy in a clinical setting

To date, no data are available from clinical trials evaluating the concomitant use of ipilimumab and RT in patients with advanced melanoma

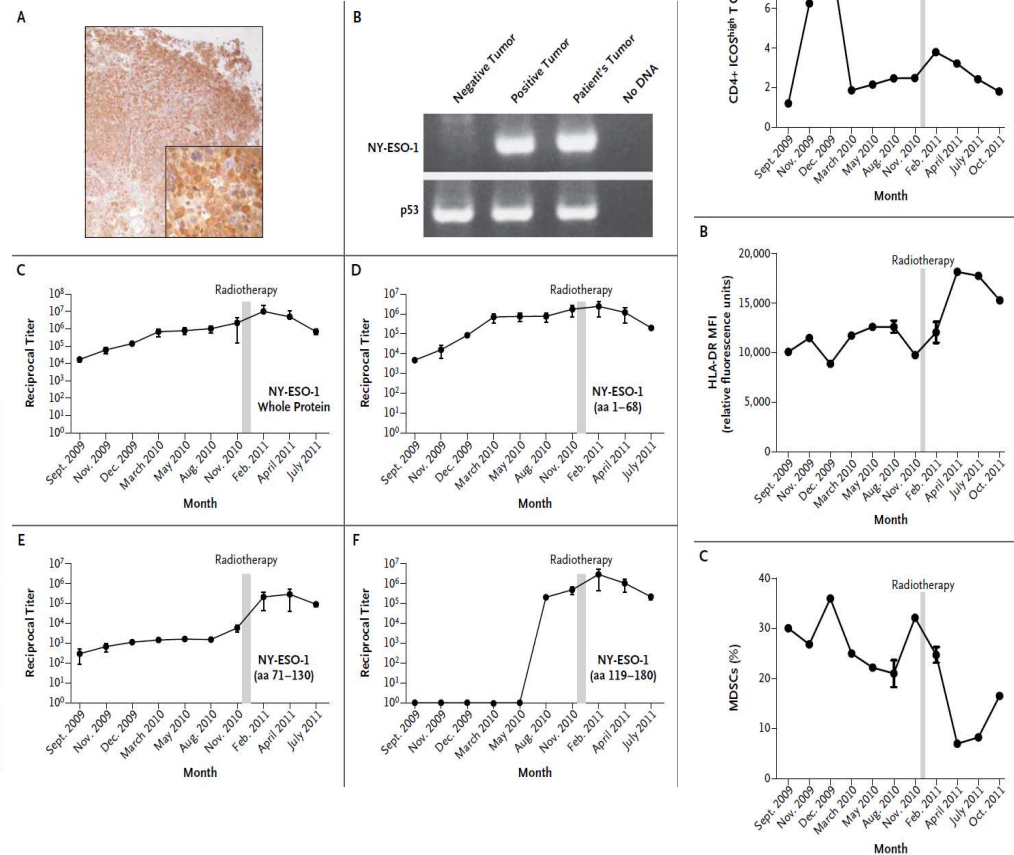
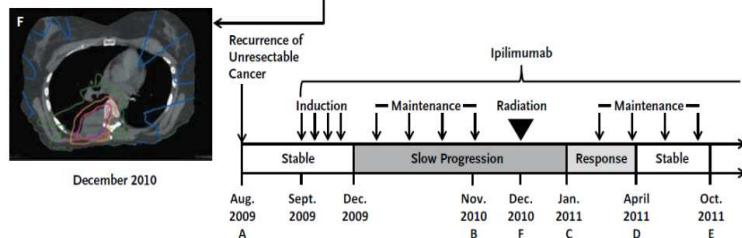
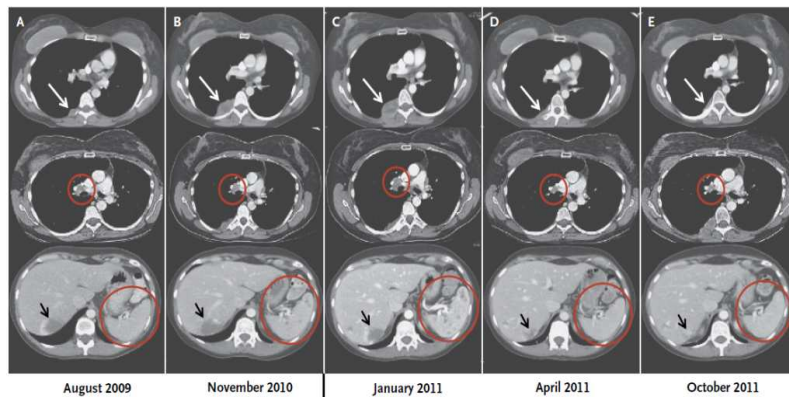
Ongoing clinical trials will help to further our understanding

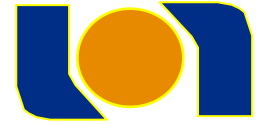


## BRIEF REPORT

# Immunologic Correlates of the Abscopal Effect in a Patient with Melanoma

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# Concept of the Study

Retrospective analysis of patients treated with ipilimumab inside the Italian expanded access program (EAP) at Istituto Tumori di Napoli to evaluate all melanoma patients who were treated with local RT after progression with Ipilimumab 3mg/kg.



# Aim of the Study

If localized RT may break out sistemic immune response in patients progressing after treatment with ipilimumab.

To identify clinical features predicting outcome of patients progressing after treatment with ipilimumab

# Patients characteristics (I)



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<b>Median age, years (range)</b>	58 years (21-77)
<b>Male/female</b>	11(52%) 10(48%)
<b>Stage III unresectable</b>	<b>0/21 pts</b>
<b>Stage IV</b>	<b>21/21 pts</b>
M1a	2 (9,5%)
M1b	2 (9,5%)
M1c	17 (81%)
<b>LDH median (range)</b>	480 (223-905)
<b>Time from diagnosis, months (range)</b>	19 (1-144)
<b>BRAF status</b>	
mutated	3 pts (15%)
WT	18 pts (85%)

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# Patients characteristics (II)



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## Number of previous therapy, n(%)

1	20 (95,3%)
2	1 (4.7%)
≥3	0

## Previous therapy type

CDDP+TMZ	5 (24%)
DTC	8 (38%)
Fotemustine	2 (9.5%)
Temozolamide	3 (14.3%)
MAGE A3	1 (4.7%)
MEK 162	1 (4.7%)
Dabrafenib	1 (4.7%)

## Time to progression from Ipilimumab, months (range)

**4 (3-6)**

## Ipilimumab cycles

4 (one patient received further 4 cycles as reinduction)	20 (95.2%)
3	1 (4.8%)

# Patients characteristics (III)



<b>Time from ipilimumab to RT, month (range)</b>	<b>5 (4-8)</b>
<b>RT site</b>	
Brain	13 (61%)
<i>WBRT</i>	8 (61.5%)
<i>SRX</i>	5 (38.5%)
Leg (Bone)	2 (9.6%)
Metastatic Distant Lymph Nodes	2 (9.6%)
Cutaneous metastasis	2 (9.6%)
Spinal Cord	2 (9.6%)



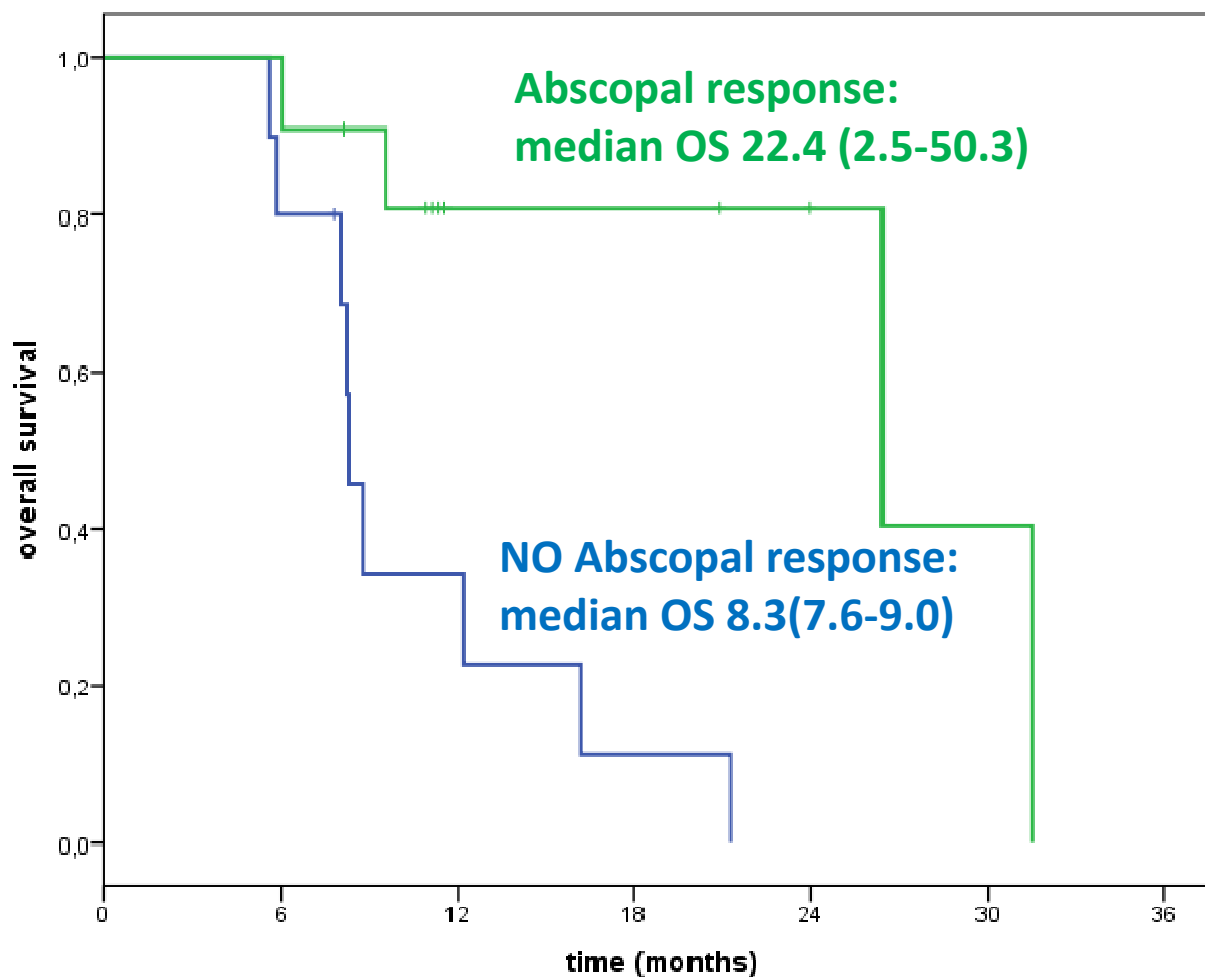
# Abscopal Response - Results

<b>Ipilimumab median PFS, months (range)</b>	<b>4 (3-6)</b>
<b>Local response to RT</b>	
Yes	<b>13 (62%)</b>
No	<b>8 (38%)</b>
<b>Immune-related response after RT (abscopal response)</b>	
Abscopal partial response	<b>9 pts (42.8%)</b>
Abscopal stable disease	<b>2 pts (9.6%)</b>
No abscopal response	<b>10 pts (47.6%)</b>
<b>Time from RT to abscopal response, months (range)*</b>	
	<b>1 (1-4)</b>
<b>Median follow-up (months)</b>	<b>11 (6-32)</b>
<b>Median OS (months)</b>	<b>13 (95% c.i. 6-26)</b>
Median OS in pts with abscopal responses (months)	<b>22.4 (2.5 - 50.3)</b>
Median OS in pts without abscopal responses (months)	<b>8.3 (7.6 – 9.0)</b>

*Grimaldi et al. manuscript in preparation*



# Survival According to Abscopal Response



P=0.002

*Grimaldi et al. manuscript in preparation*

# Conclusions



First retrospective analysis of patients treated with RT after ipilimumab failure.

11/21 pts (52,4%) obtained an Abscopal Response recovering a “Lost Response” with RT, with also improvement in Quality of Life .

Local Response to RT may be predictive of Abscopal Response. 11 (85%) out of 13 pts with Local Response, obtained an Abscopal Effect

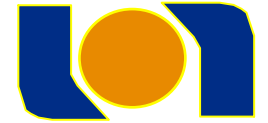
# Conclusions



Median OS for patients with Abscopal Response resulted 22.4 months while mOS for patients that did not obtain Abscopal Response resulted 8.3 months

Our data confirm that RT after Ipilimumab may represent a therapeutic option for metastatic melanoma patients after ipi failure.

Sinergism of Ipilimumab and Radiotherapy need prospective validation in clinical trials.

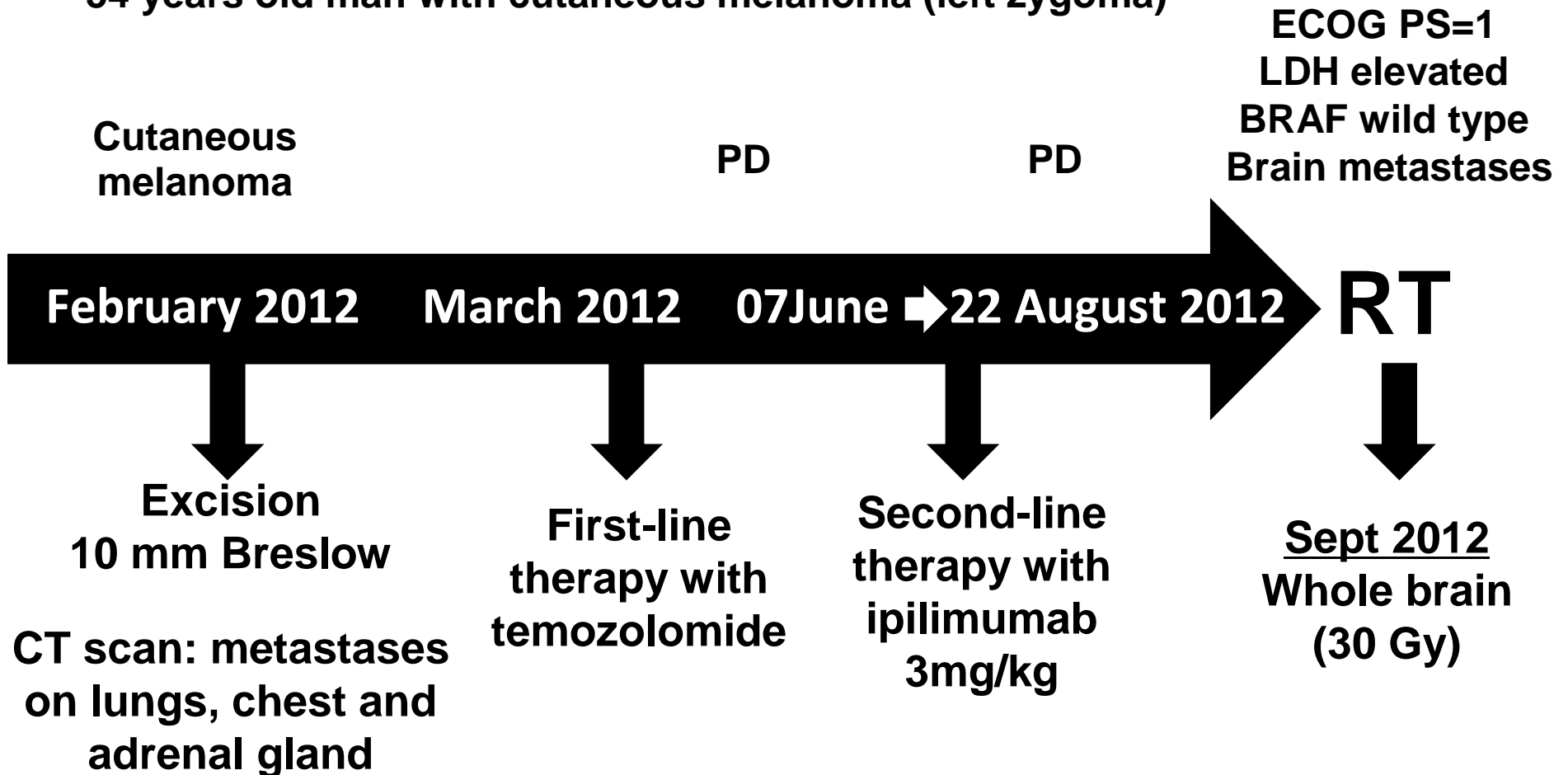


# Clinical Cases

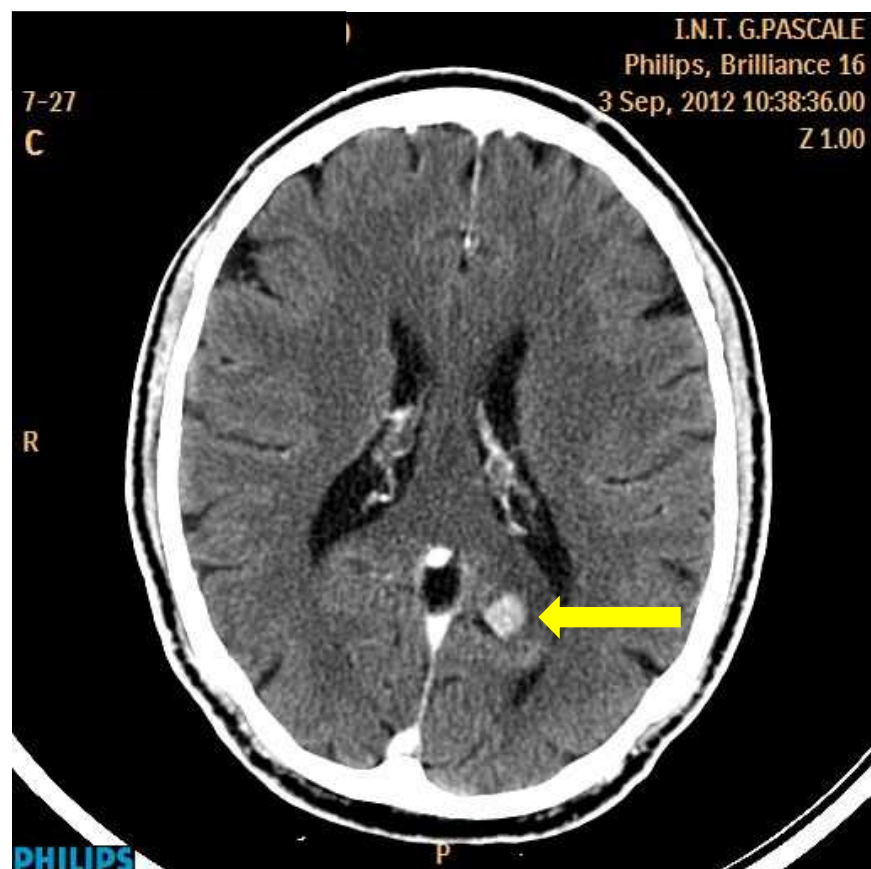


# Abscopal Effect Clinical Case 1

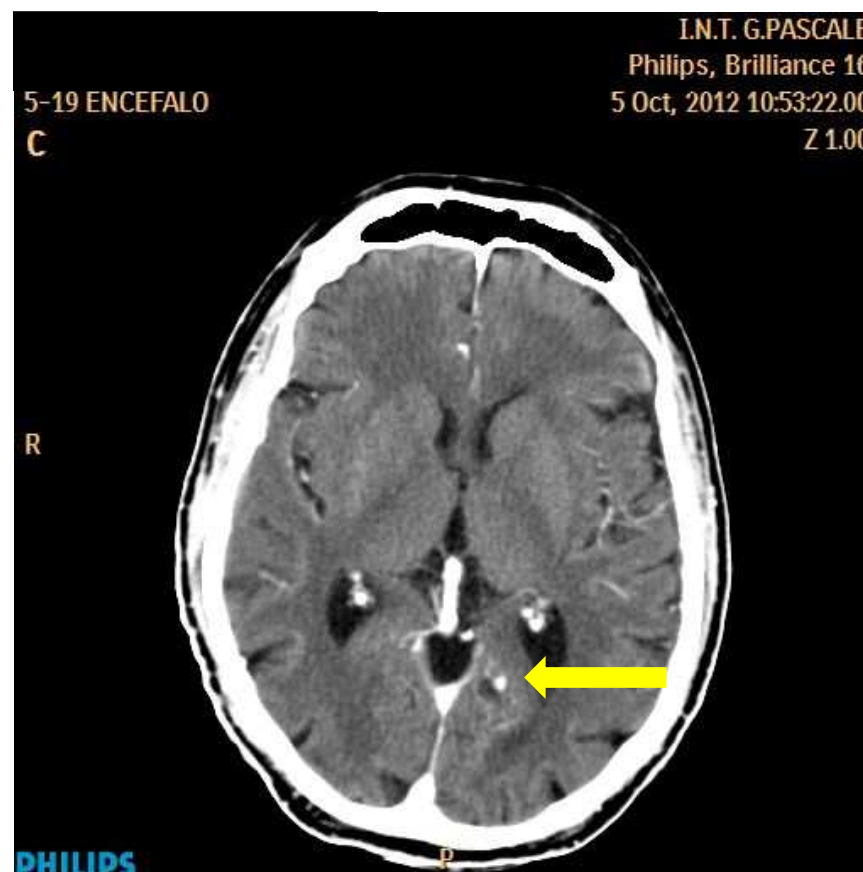
54 years old man with cutaneous melanoma (left zygoma)



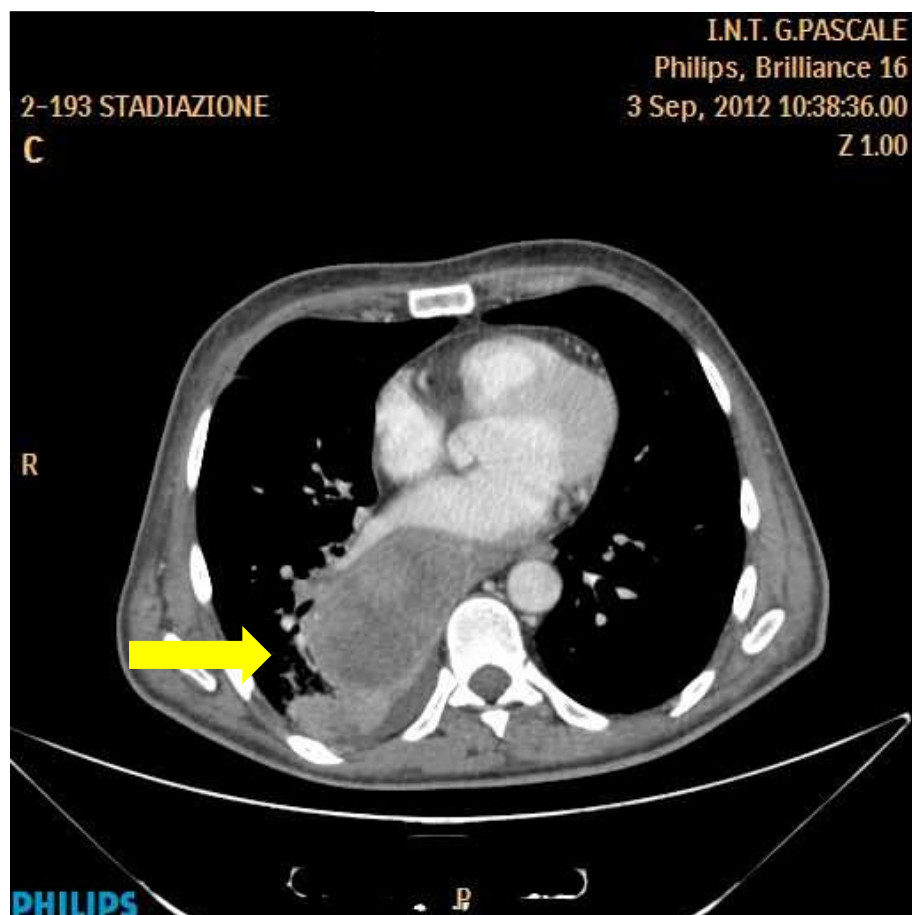




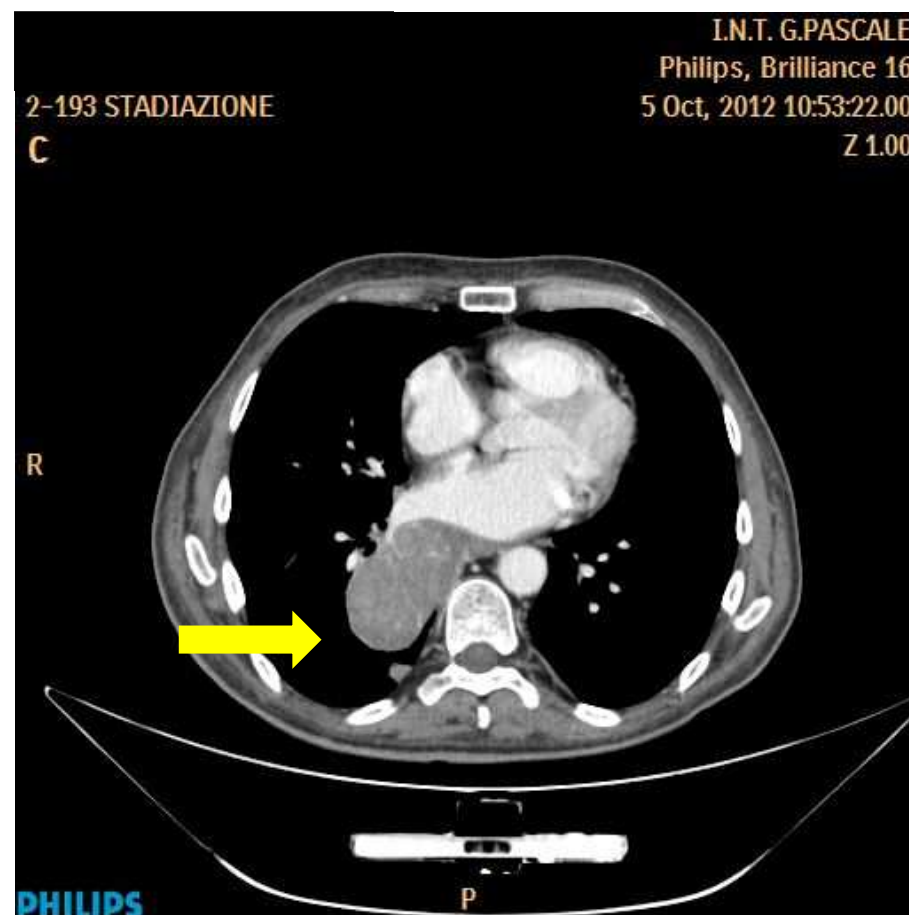
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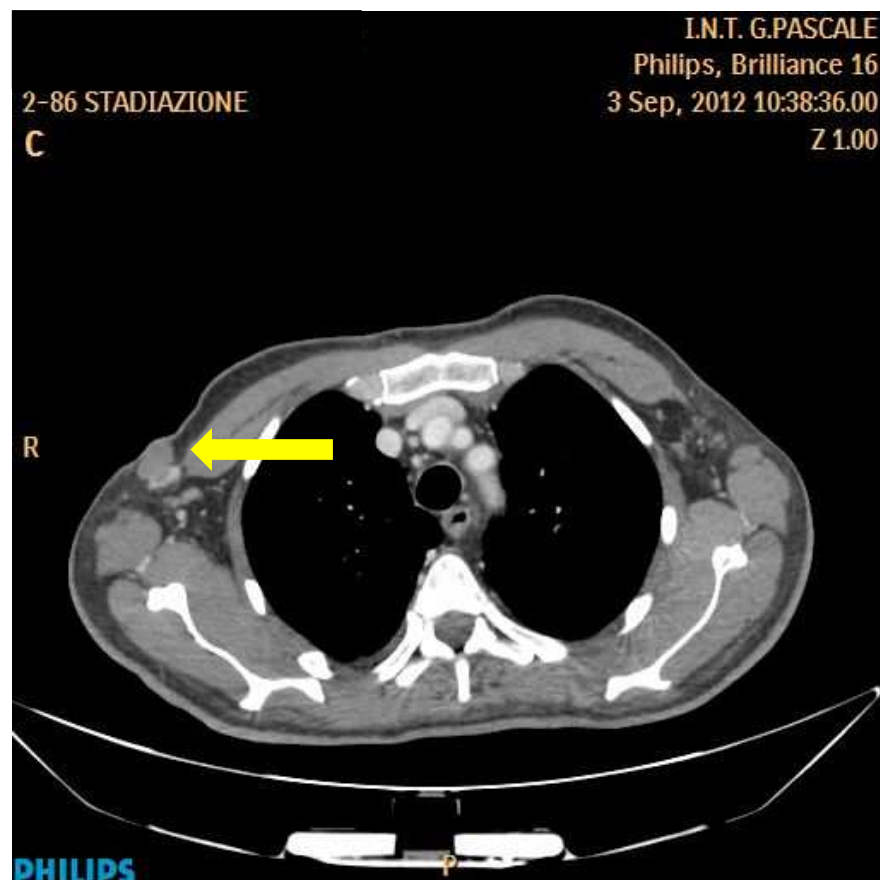


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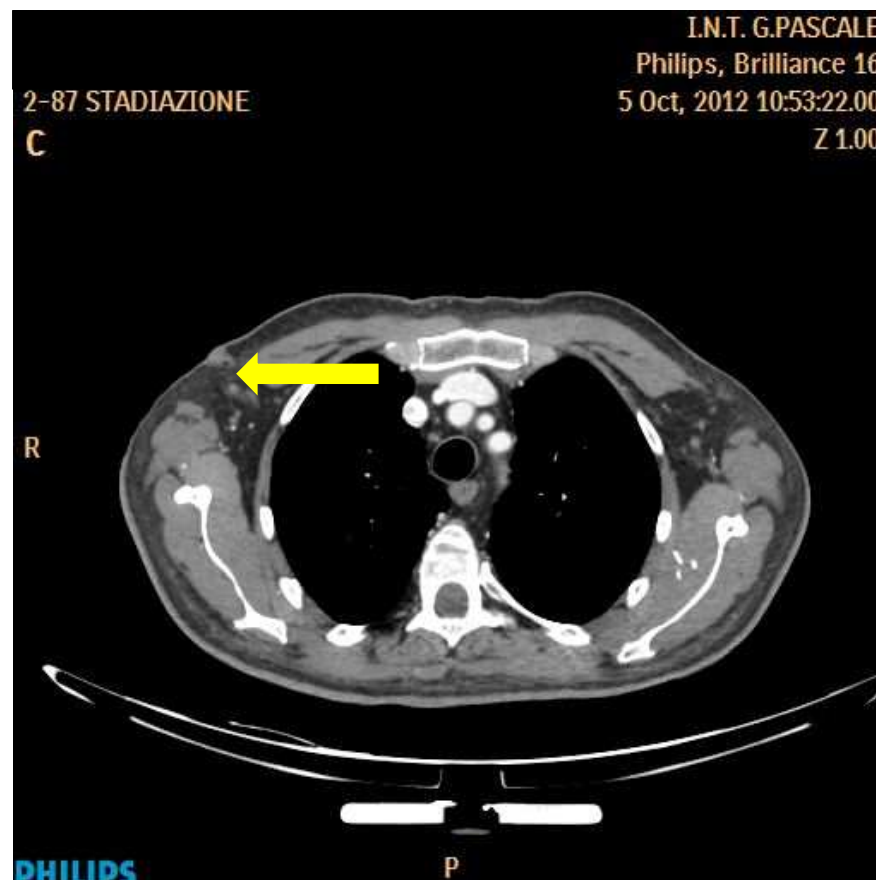


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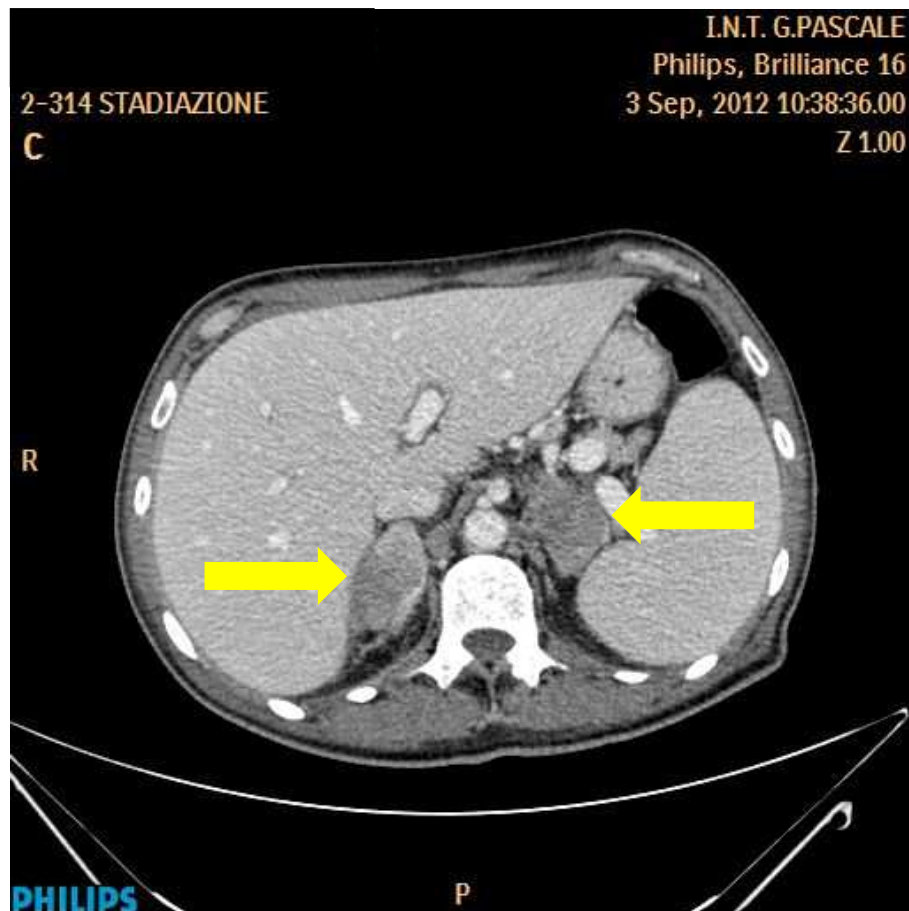
*Courtesy of Dr P.A. Ascierto – Istituto Nazionale Tumori Napoli*



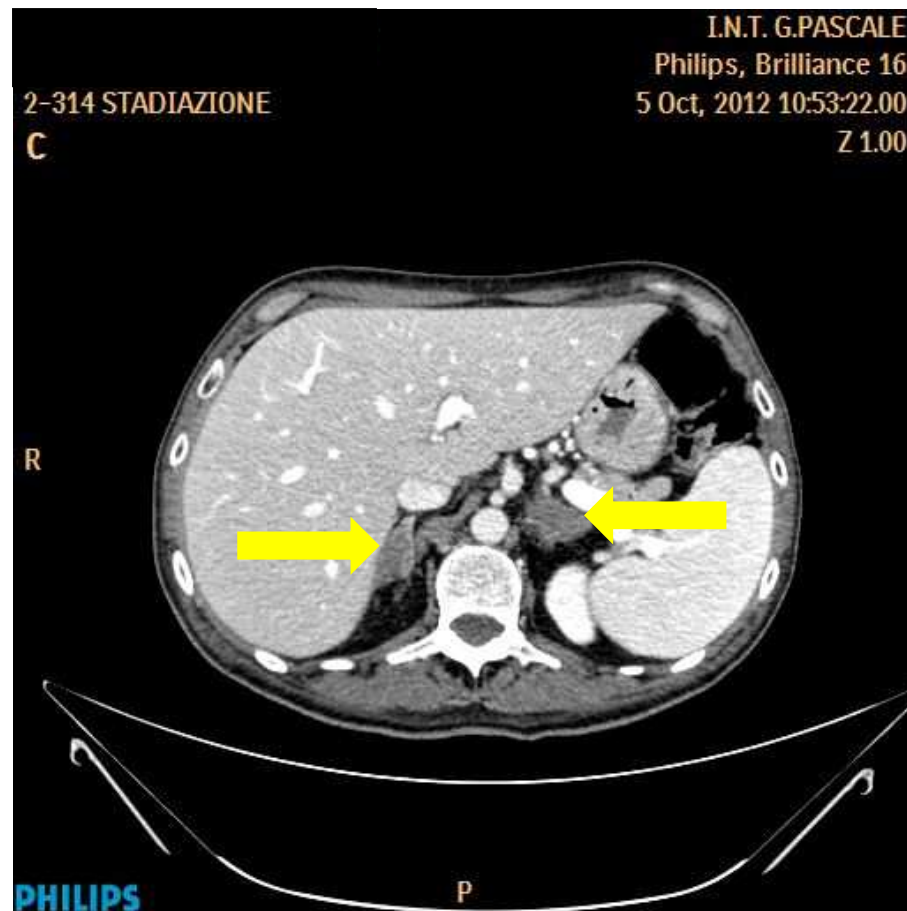
SEPT 2012



05 OCT 2012



SEPT 2012



05 OCT 2012

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# Abscopal Effect Clinical Case 2

52 years old woman with cutaneous melanoma (trunk)

ECOG PS=1  
LDH elevated  
BRAF wild type  
Brain, breast and  
abdominal  
metastases

Feb '11: excision  
cutaneous melanoma  
8 mm Breslow

PD

PD

January 2012

March 2012

29 May

01 August 2012

RT

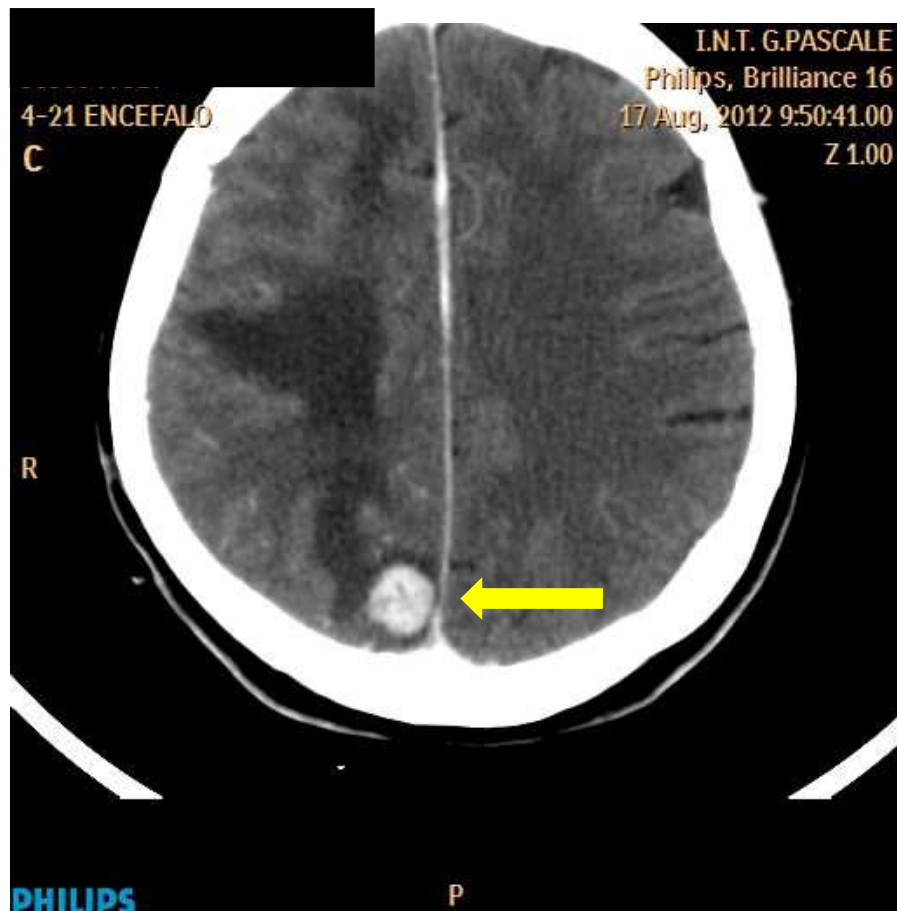
CT scan: evidence  
of skin and  
diffuse lymphnodal  
metastases

First-line  
therapy with  
dacarbazine

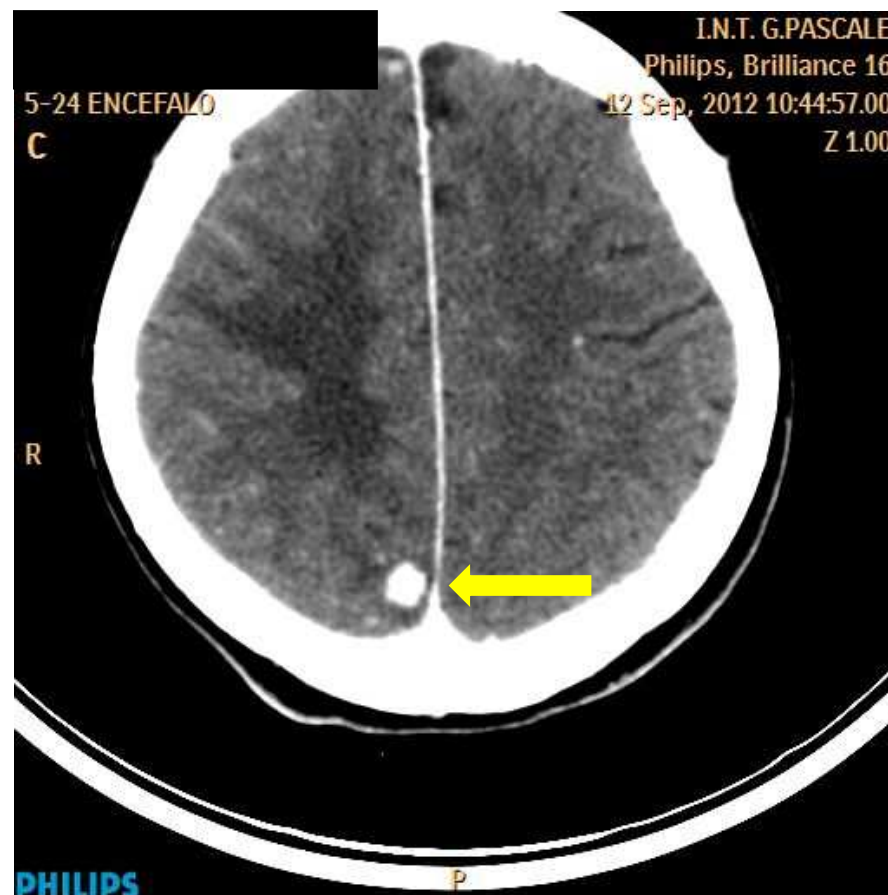
Second-line  
therapy with  
ipilimumab  
3mg/kg

Aug-Sept 2012  
Whole brain  
(30 Gy)



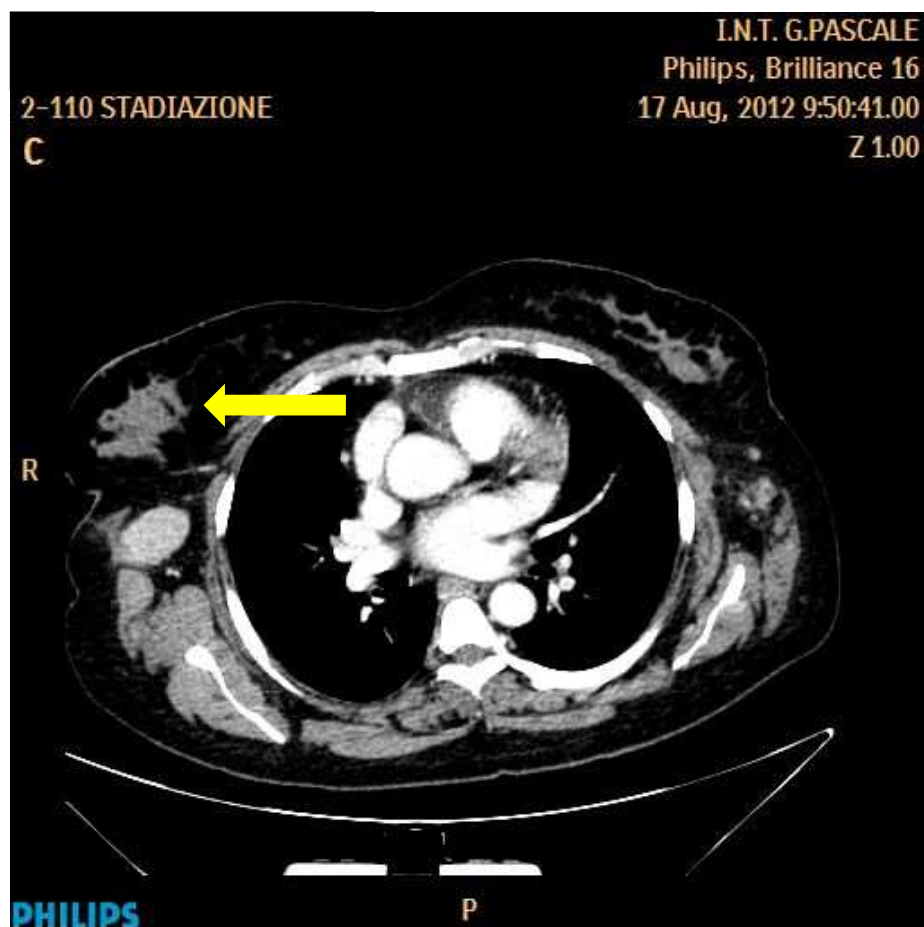


17 AUG 2012

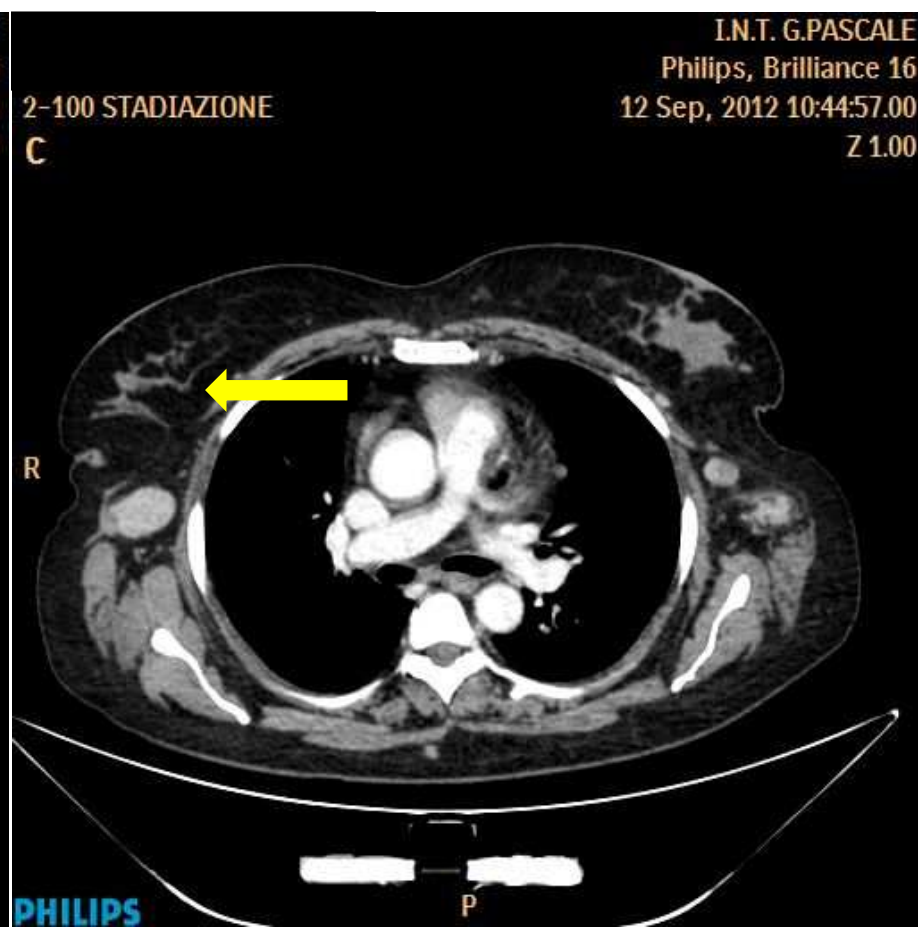


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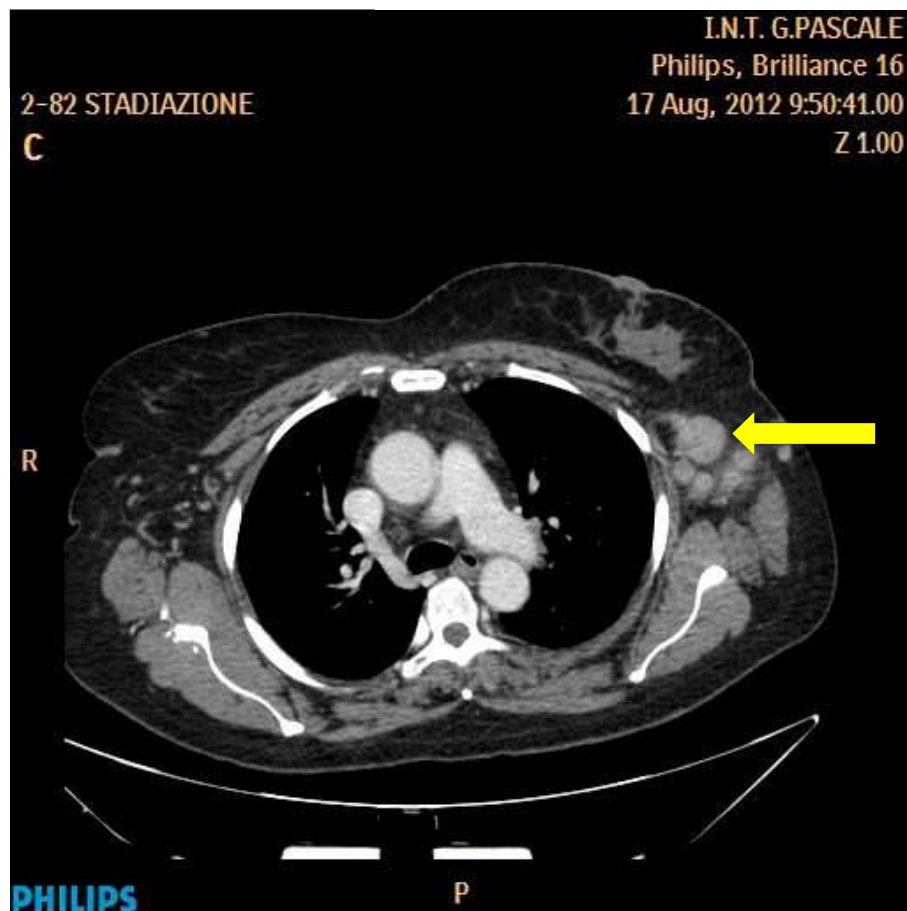
*Courtesy of Dr P.A. Ascierto – Istituto Nazionale Tumori Napoli*



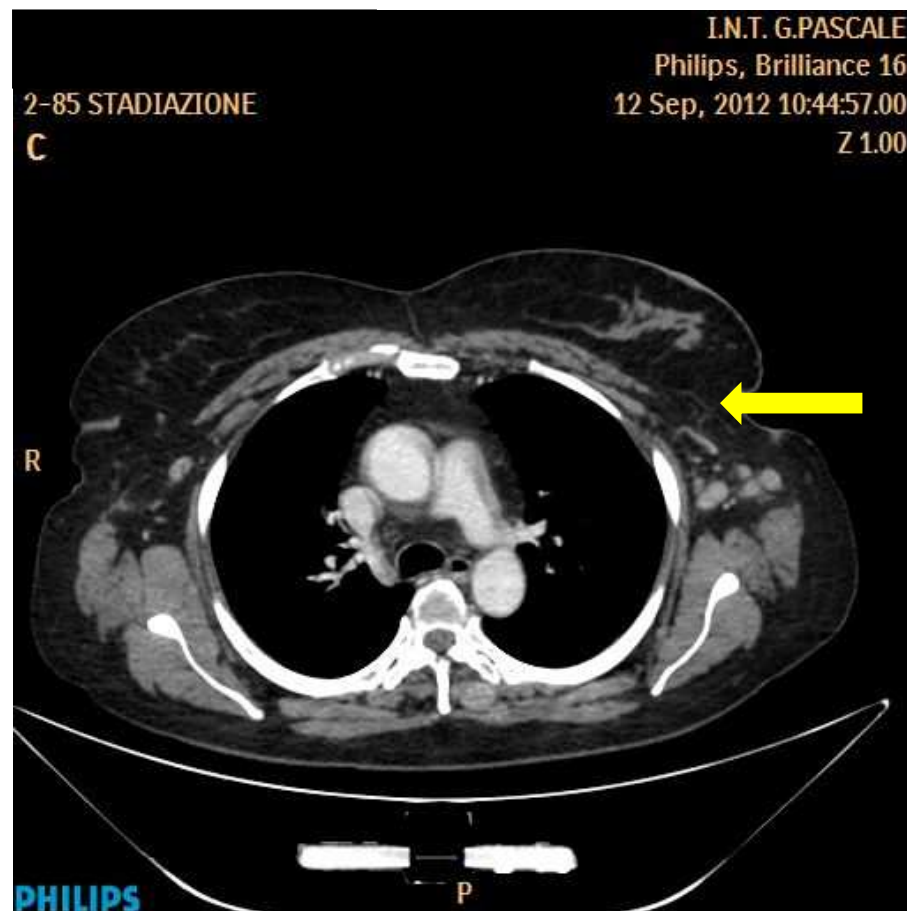
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*Courtesy of Dr P.A. Ascierto – Istituto Nazionale Tumori Napoli*





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