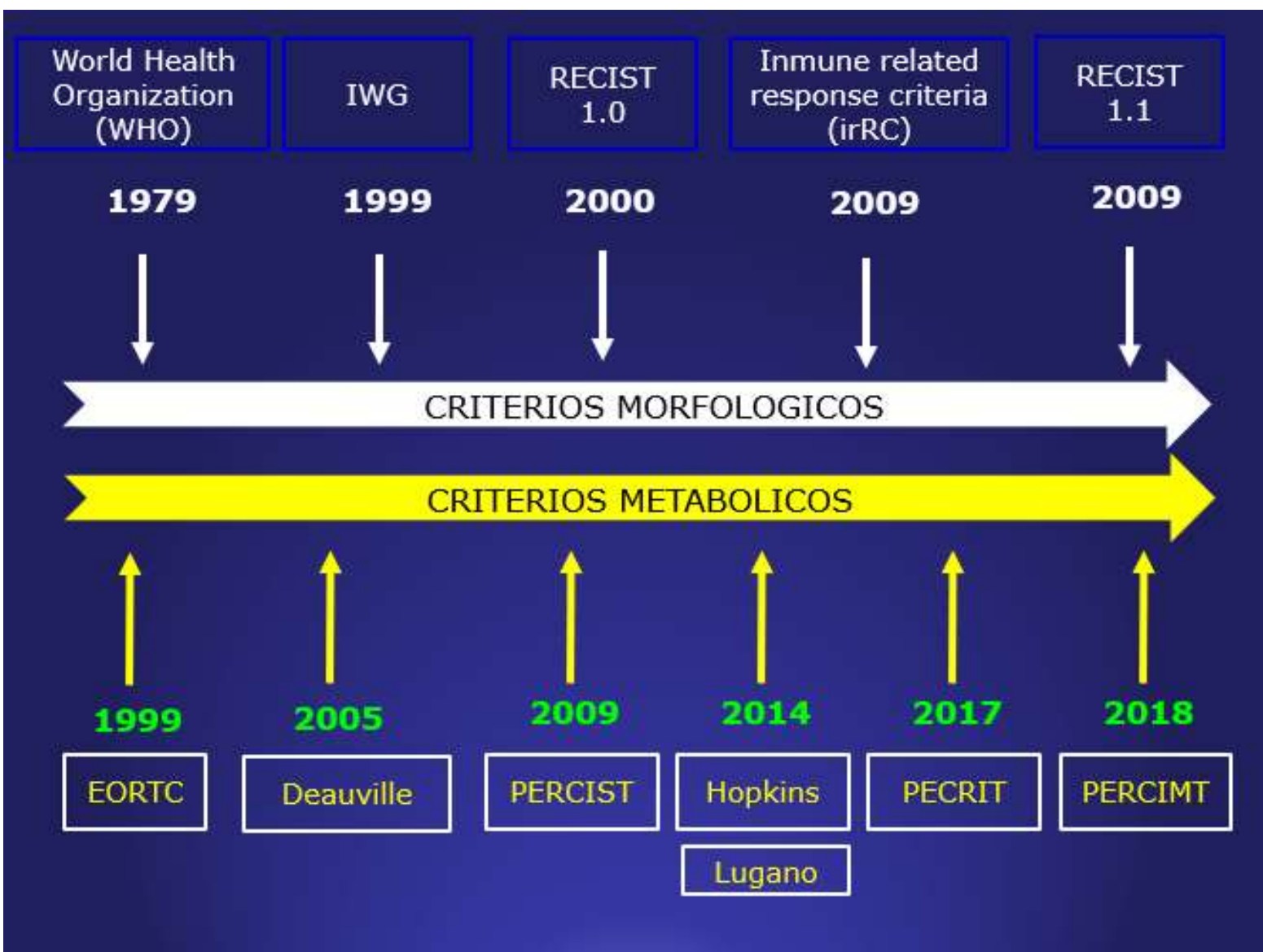




CRITERIOS DE RESPUESTA METABOLICA PET-TC EN TUMORES SOLIDOS: PERCIST- HOPKINS

Antonio Maldonado Suarez, Raquel Cano Alonso,
Eric Alexander Rodriguez Gallo, Ana Alvarez
Vazquez, Ana Fernandez Alfonso,
Chawar Hayoun, Javier Carrascoso Arranz,
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Hospital Universitario Quirónsalud Madrid, Pozuelo
de Alarcón



Valoración de respuesta al tratamiento

| | | |
|----------------------|--|----------------|
| Moertel y Hanley | <i>Cancer 1976;38:388-394</i> | Datos clínicos |
| Criterios WHO | <i>Cancer 1981;47:207-214</i> | Datos clínicos |
| Criterios RECIST | <i>J Nat Cancer Inst 2000;92:205-216</i> | CT/RM |
| Criterios RECIST 1.1 | <i>Eur J Cancer 2009;45:228-247</i> | CT/RM |

Criterios standard en la valoración de respuesta en ensayos clínicos

Criterios RECIST 1.1

- Limitaciones para valorar respuesta en algunos tumores por la discordancia entre la respuesta según criterios RECIST y la supervivencia/intervalo libre de enfermedad al tratamiento
 - GIST- Criterios Choi (*J Clin Oncol* 2007; 25:1760-64)
 - HCC- Criterios EASL (*Cancer* 2009; 115:616-23)



IMAGEN METABOLICA PET

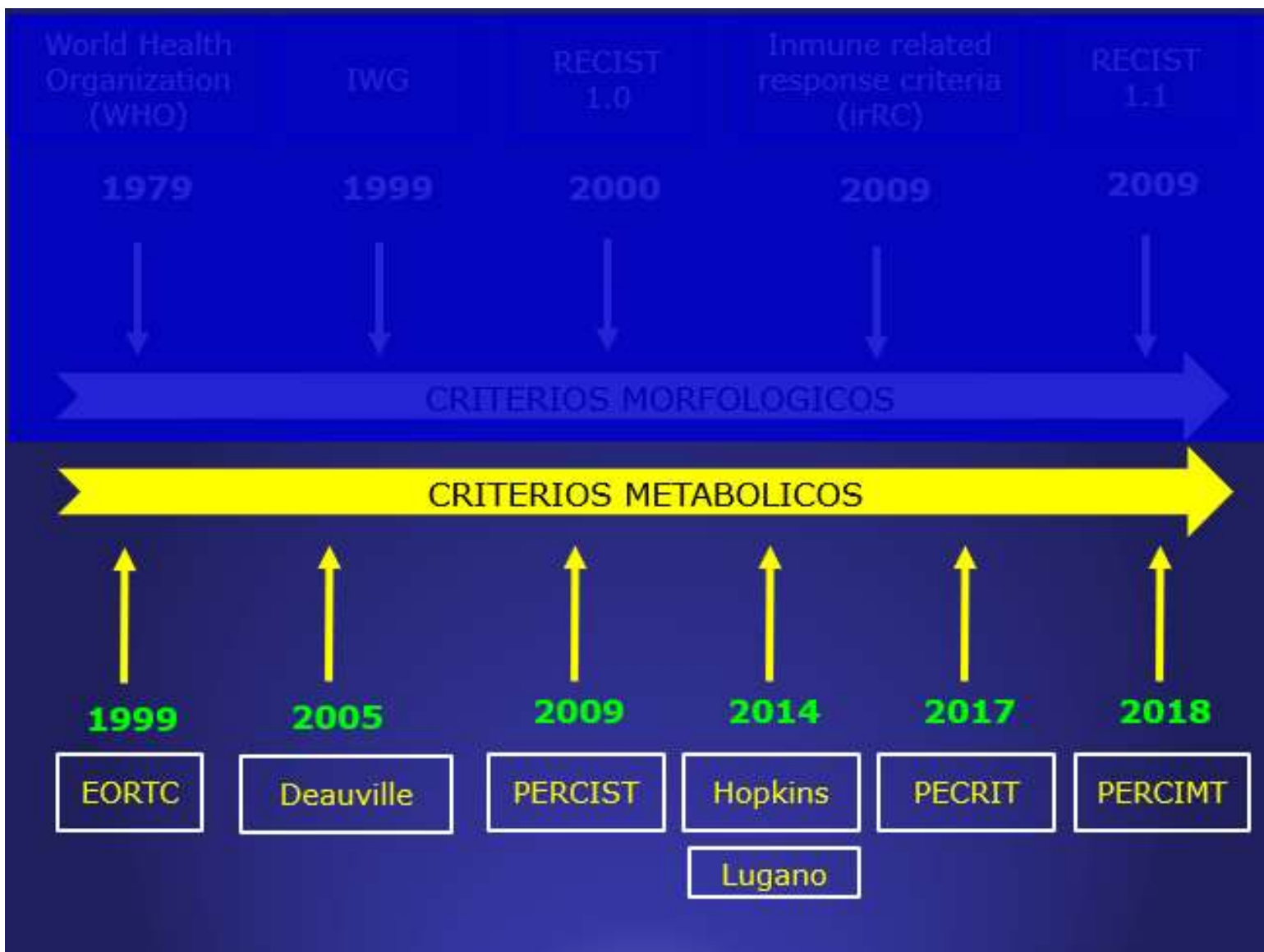


Imagen metabólica PET

- **1993**: inicio del uso de la cuantificación de la imagen PET-FDG para valorar respuesta al tratamiento (*JCO 1993;11: 2101-11*)
- Diferencia de forma precoz respondedores/no respondedores por descenso SUV (*N Eng J Med 2006; 354:496-507 / EJNM 2006; 33:27-37*)
- Útil para valorar respuesta precoz al tratamiento en muchos tumores sólidos.
Importante → Estudio basal / inter-tratamiento/ post-tratamiento



Cancer 2007; 110:1738-44
JCO 2006;24:3282-3292
JNM 2006;47; 901-3

PET: predecir la respuesta y valorar la eficacia de los tratamientos en cuanto a índices de supervivencia e intervalo libre de enfermedad

Personalizar respuesta al tratamiento según tipo de cáncer y de terapia

Curr Opin Pharmacol 2012 Oct 12(5):569-75
AJR 2012 April 118(4):737-45

Descenso FDG → Descenso de células cancerígenas viables
Aumento captación FDG → Progresión tumoral

- PET negativo tras tratamiento

- Buen pronóstico. Mayor supervivencia e intervalo libre de enfermedad. No hay células cancerígenas presentes o como mucho 10^8
- Resolución equipos PET (4-5mm) equivale a $0,1-05 \text{ gr}/10^8-10^9$ células
- **Limitación:** enfermedad microscópica (*J Clin Oncol 2008;26:11-28-34/Leuven Group*)

- PET positivo tras tratamiento: altamente sugestivo de tumor

- La captación de FDG desciende más rápidamente que el tamaño tumoral en caso de respuesta al tratamiento (*JNM 2005; 46: 983-95*)
- Es frecuente que el PET se normalice más rápidamente que los cambios anatómicos

PET en la valoración de respuesta

| Autor | Revista | Año | N | Enf. Residual Sb | Enf. residual Ep | Descenso SUV |
|-----------------|-----------------|------|------------|---------------------|---------------------|-----------------|
| <u>Bury</u> | Eur Resp J | 1999 | 126 | 100 | 92 | |
| <u>Eschmann</u> | JNM | 2007 | 70 | 95 | 80 | > 80% |
| <u>Cerfolio</u> | Ann Thorac Surg | 2004 | 56 | 90 | - | > 80% |
| <u>Pottgen</u> | Clin Cancer Res | 2006 | 80 | - | - | 50% |
| <u>Weber</u> | J Clin Oncol | 2003 | 41 | 96 | 97 | 20% |
| | | | 373 | 95% | 89,6% | |

Limitación: detección de la enfermedad microscópica

PET: técnica que permite cuantificación absoluta

S.U.V: Standard Uptake Value

Refleja la **captación de FDG** expresada en función de la **dosis** inyectada, del **tiempo** transcurrido entre la administración y el comienzo del estudio y del **peso** del paciente.

median ROI activity (MBq/ml)

$$\text{SUV: } \frac{\text{median ROI activity (MBq/ml)}}{\text{Injected dose (MBq/ml)/body weight (gr)}}$$

SUL: SUV normalizado por la masa corporal

TLG: Total Lesion Glycolysis- volumen de la lesión y actividad metabólica

Criterios de respuesta metabólica PET

Importante una **rigurosa standardización de los estudios** tanto basales como inter y post-tratamiento que permitan reproductibilidad de los estudios (*JNM 2006 47;1059-66*)

- Preparación del paciente
- Dosis inyectada
- Tiempo de adquisición
- Realizar en mismo equipo los distintos estudios
- Tamaño del ROI para cálculo del SUV, etc.....



La cuantificación es superior a la valoración visual para valorar respuesta pero necesaria una rigurosa estandarización tanto en la adquisición como en el análisis cuantitativo



World Health Organization (WHO)

1979

IWG

1999

RECIST 1.0

2000

Immune related response criteria (irRC)

2009

RECIST 1.1

2009

CRITERIOS MORFOLOGICOS

CRITERIOS METABOLICOS

1999

EORTC

2005

Deauville

Lugano

2009

PERCIST

2014

Hopkins

2017

PERCIT

2018

PERCIMT

Criterios de respuesta EORTC-1999

- **Enfermedad metabólica Progresiva**
 - aumento SUV ($> 25\%$) respecto basal
 - aumento del tamaño de captación ($> 20\%$)
 - aparición de nuevas captaciones
- **Enfermedad metabólica Estable**
 - aumento SUV $< 25\%$ o disminución $< 15\%$ y no aumento de la captación
- **Respuesta metabólica Parcial**
 - disminución SUV (15-25%) tras 1º ciclo QT y $> 25\%$ después de más ciclos
- **Respuesta metabólica Completa**
 - resolución completa de la captación anómala

EORTC PET Response Criteria (*Eur J Cancer* 1999; 35:1773-82)

World Health Organization (WHO)

1979

IWG

1999

RECIST 1.0

2000

Immune related response criteria (irRC)

2009

RECIST 1.1

2009

CRITERIOS MORFOLOGICOS

CRITERIOS METABOLICOS

1999

EORTC

2005

Deauville

Lugano

2009

PERCIST

2014

Hoplans

2017

PECRIT

2018

PERCIMT

Criteria PERCIST 1.0

JNM

Volume 50, Supplement 1 • May 2009

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1035 From RECIST to PERCIST: Evolving Considerations for PET Response Criteria in Solid Tumors
Richard L. Wahl^{1,2}, Heather Jacene¹, Yvette Kasamon², Yvonne Kassarjian, and Martin A. Lodge¹

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Supplement to
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Personalizing Cancer Therapy with PET: From RECIST to PERCIST

SNM

From RECIST to PERCIST: Evolving Considerations for PET Response Criteria in Solid Tumors

Richard L. Wahl^{1,2}, Heather Jacene¹, Yvette Kasamon², and Martin A. Lodge¹

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The purpose of this article is to review the status and limitations of anatomic tumor response metrics including the World Health Organization (WHO) criteria, the Response Evaluation Criteria in Solid Tumors (RECIST), and RECIST 1.1. This article also reviews qualitative and quantitative approaches to metabolic tumor response assessment with ¹⁸F-FDG PET and proposes a draft framework for PET Response Criteria in Solid Tumors (PERCIST), version 1.0. **Methods:** PubMed searches, including searches for the terms RECIST, positron, WHO, FDG, cancer (including specific types), treatment response, region of interest, and derivative references, were performed. Abstracts and articles judged most relevant to the goals of this report were reviewed with emphasis on limitations and strengths of the anatomic and PET approaches to treatment response assessment. On the basis of these data and the authors' response assessment, draft criteria were formulated for PET tumor response to treatment. **Results:** Approximately 3,000 potentially relevant references were screened. Anatomic imaging alone using standard WHO, RECIST, and RECIST 1.1 criteria is widely applied but still has limitations in response assessments. For example, despite effective treatment, changes in tumor size can be minimal in tumors such as lymphomas, sarcomas, hepatomas, mesotheliomas, and gastrointestinal stromal tumor. CT tumor density, contrast enhancement, or MRI characteristics appear more informative than size but are not yet routinely applied. RECIST criteria may show progression of tumor more slowly than WHO criteria.

3-cm-diameter region of interest in the liver, using a consistent PET protocol, using a fixed small region of interest about 1 cm³ in volume (1.2-cm diameter) in the most active region of metabolically active tumors to minimize statistical variability, assessing tumor size, treating SUV lean measurements in the 1 (to 5.0) (arbitrary) most metabolically active tumor focus as a continuous variable, requiring a 30% decline in SUV for "response," and deferring to RECIST 1.1 in cases that do not have ¹⁸F-FDG avidity or are technically unsuitable. Criteria to define progression of tumor-abrupt new lesions are uncertain but are proposed. **Conclusions:** Anatomic imaging alone using standard WHO, RECIST, and RECIST 1.1 criteria have limitations, particularly in assessing the activity of newer cancer therapies that stabilize disease, whereas ¹⁸F-FDG PET appears particularly valuable in such cases. The proposed PERCIST 1.0 criteria should serve as a starting point for use in clinical trials and in structured quantitative clinical reporting. Undoubtedly, subsequent revisions and enhancements will be required as validation studies are undertaken in varying diseases and treatments.

Key Words: molecular imaging; oncology; PET/CT; anatomic imaging; RECIST; response criteria; SUV; treatment monitoring
J Nucl Med 2009; 50:1228-1268
DOI: 10.2967/jnumed.108.067307



Criterios PERCIST 1.0

- **PERCIST: PET Response Criteria In Solid Tumors**
- Propuestos por Wahl en 2009 para poder utilizar la PET en la valoración de la respuesta en ensayos clínicos y de forma opcional en la práctica diaria (*JNM 2009:50:122S-150S*)
- No intervino el comité RECIST en su elaboración
- Estudios PET según recomendaciones del NCI y del grupo multicéntrico holandés (*JNM 2006 47:1059-66*)
 - Ayunas 4-6 horas /Glucemia < 200 mgr/dl
 - Pueden tomar antidiabéticos orales. No insulina
 - PET a los 50-70 min post-inyección
 - Todos los estudios en el mismo equipo PET y con la misma dosis (+/- 20%)
 - Obtener el SUL (SUV corregido por la masa corporal)
 - Referencia el lóbulo hepático derecho (ROI de 3 cm)
 - Determinan el SUL en hasta 5 tumores por órgano. Pico de máxima intensidad
 - La respuesta se basa en el cambio del SUV peak

Respuesta completa

Respuesta parcial: si hay descenso SUL >30%

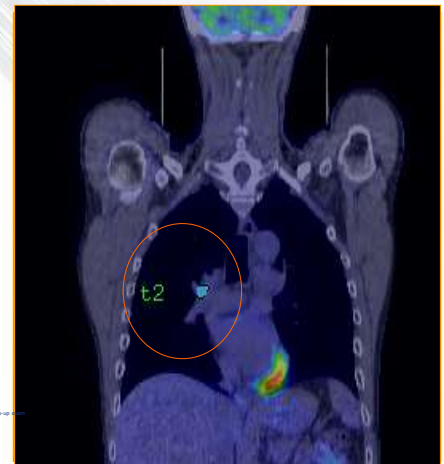
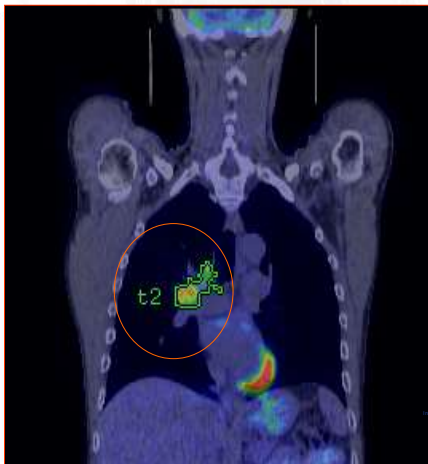
Progresión tumoral: incremento SUL > 30%

PERCIST

CRITERIOS DE RESPUESTA METABOLICA

| Lesion [#] | Status / Type | | Functional Volume [cm ³] | | Functional Volume Change [%] | | SUV Max [SUVbw g/ml] | | SUV Max Change [%] | |
|------------|---------------------|---------------------|--------------------------------------|------------|------------------------------|------------|----------------------|------------|--------------------|------------|
| | 2007-04-05 | 2007-06-05 | 2007-04-05 | 2007-06-05 | 2007-04-05 | 2007-06-05 | 2007-04-05 | 2007-06-05 | 2007-04-05 | 2007-06-05 |
| 1 | Accepted Metastatic | Accepted Metastatic | 32.9 | 0.1 | -99.7 | 9.9 | 2.2 | - | -97.7 | |
| 2 | Accepted Metastatic | Accepted Metastatic | 42.4 | 0.7 | -98.4 | 9.7 | 3.0 | - | -98.4 | |
| 3 | Accepted Tumor | Accepted Tumor | 64.9 | 48.9 | -24.7 | 24.6 | 21.9 | - | -11.1 | |
| Summary | - | - | 140.2 | 49.7 | -64.6 | 24.6 | 21.9 | - | -11.1 | |

■ PD: Progressive disease
 ■ SD: Stable disease
 ■ PR: Partial response



Show Columns

Parameter Columns:

- Status / Type
- Functional Volum
- SUV Max
- GN SUV Max
- BN SUV Max
- SUV Mean
- GN SUV Mean
- BN SUV Mean
- TLG
- GN TLG
- Long Axis
- Product of Diam
- Slice Number
- RAS Coordinates

Exam Columns:

- EORTC
- Custom
- None

| Lesion [#] | Status / Type | | Functional Volume [cm³] | | Functional Volume C... [%] | | SUV Max [SUVbw g/ml] | | TLG [SUVbw g] | | TLG Change [%] | | Slice Numbr [#] |
|------------|---------------|-------------|-------------------------|------------|----------------------------|------------|----------------------|------------|---------------|------------|----------------|------------|-----------------|
| | 2006 06-20 | 2006 08-29 | 2006 06-20 | 2006 08-29 | 2006 06-20 | 2006 08-29 | 2006 06-20 | 2006 08-29 | 2006 06-20 | 2006 08-29 | 2006 06-20 | 2006 08-29 | |
| 1 | N | N | 0.6 | 0.0 | - | -100.0 | 6.1 | - | 3.4 | - | - | -100.0 | 81 |
| 2 | N | N | 1.2 | 0.0 | - | -100.0 | 10.2 | - | 8.5 | - | - | -100.0 | 89 |
| 3 | N | N | 4.4 | 0.0 | - | -100.0 | 13.7 | - | 29.5 | - | - | -100.0 | 110 |
| 4 | T | T | 21.6 | 0.7 | - | -96.7 | 12.4 | 9.3 | 139.3 | 4.1 | - | -97.1 | 114 |
| 5 | N | N | 14.2 | 0.0 | - | -100.0 | 12.6 | - | 100.7 | - | - | -100.0 | 112 |
| 6 | N | N | 1.1 | 0.0 | - | -100.0 | 7.6 | - | 6.1 | - | - | -100.0 | 114 |
| 7 | T | T | 6.3 | 0.0 | - | -100.0 | 8.4 | - | 34.3 | - | - | -100.0 | 125 |
| 8 | T | T | 8.6 | 0.0 | - | -100.0 | 11.8 | - | 59.4 | - | - | -100.0 | 129 |
| 9 | T | T | 18.8 | 3.2 | - | -83.1 | 10.2 | 13.0 | 116.8 | 22.0 | - | -81.1 | 133 |
| 10 | T | Inflamma... | 47.9 | 1.1 | - | -97.6 | 13.0 | 13.0 | 329.6 | 11.1 | - | -96.6 | 138 |
| 11 | - | Inflamma... | - | 45.2 | - | ∞ | - | 41.7 | - | 1233.2 | - | ∞ | - |
| Summary | | | 124.6 | 50.2 | - | -59.7 | 13.7 | 41.7 | 827.7 | 1270.4 | - | 53.5 | - |

■ PD: Progressive disease
 ■ SD: Stable disease
 ■ PR: Partial response
 ■ CR: Complete response



■ PD: Progressive disease
 ■ SD: Stable disease
 ■ PR: Partial response
 ■ CR: Complete response

| Lesion | Status / Type | | Functional Volume [cm3] | | Functional Volume change [%] | | SUV Max [SUVbw g/ml] | | SUV Max change [%] | | SUV Mean [SUVbw g/ml] | | SUV Mean change [%] | | TLG [SUVbw g] | | TLG change [%] | | Slice Number | |
|---------|---------------|------------|-------------------------|------------|------------------------------|------------|----------------------|------------|--------------------|------------|-----------------------|------------|---------------------|------------|---------------|------------|----------------|------------|--------------|------------|
| | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 | 2007-07-16 | 2007-10-26 |
| 1 | N | N | 8.3 | 0.0 | - | -100.0 | 5.6 | - | - | -100.0 | 3.1 | - | - | -100.0 | 26.2 | - | - | -100.0 | 89 | 120 |
| 2 | T | T | 115.0 | 10.5 | - | -90.9 | 13.5 | 3.4 | - | -74.6 | 5.2 | 2.5 | - | -52.6 | 602.0 | 26.0 | - | -95.7 | 88 | 115 |
| 3 | M | M | 5.7 | 0.0 | - | -100.0 | 6.4 | - | - | -100.0 | 3.4 | - | - | -100.0 | 19.6 | - | - | -100.0 | 97 | 130 |
| 4 | M | M | 4.1 | 14.3 | - | 249.1 | 7.3 | 9.9 | - | 34.8 | 3.4 | 4.2 | - | 23.2 | 13.9 | 59.7 | - | 330.0 | 143 | 172 |
| 5 | M | M | 12.1 | 34.8 | - | 188.1 | 7.0 | 8.1 | - | 15.0 | 3.9 | 4.2 | - | 7.5 | 47.1 | 145.9 | - | 209.6 | 174 | 201 |
| 6 | M | M | 5.7 | 0.0 | - | -100.0 | 5.4 | - | - | -100.0 | 3.2 | - | - | -100.0 | 18.0 | - | - | -100.0 | 212 | 223 |
| Summary | - | - | 151.0 | 50.6 | - | -60.5 | 13.5 | 9.9 | - | -26.9 | 4.8 | 3.9 | - | -19.3 | 726.9 | 231.6 | - | -68.1 | - | - |

CR: Complete response

Lesion 1

| Date | Best illustration of finding | | |
|------------|------------------------------|--------|----------|
| | AxialS | AxialS | CoronalS |
| 2007-10-26 | | | |
| | Comment: - | | |
| 2007-07-16 | | | |

World Health Organization (WHO)

1979

IWG

1999

RECIST 1.0

2000

Immune-related response criteria (irRC)

2009

RECIST 1.1

2009

CRITERIOS MORFOLOGICOS

CRITERIOS METABOLICOS

1999

EORTC

2005

Deauville

Lugano

2009

PERCIST

2014

Hopkins

Lugano

2017

PECRIT

2018

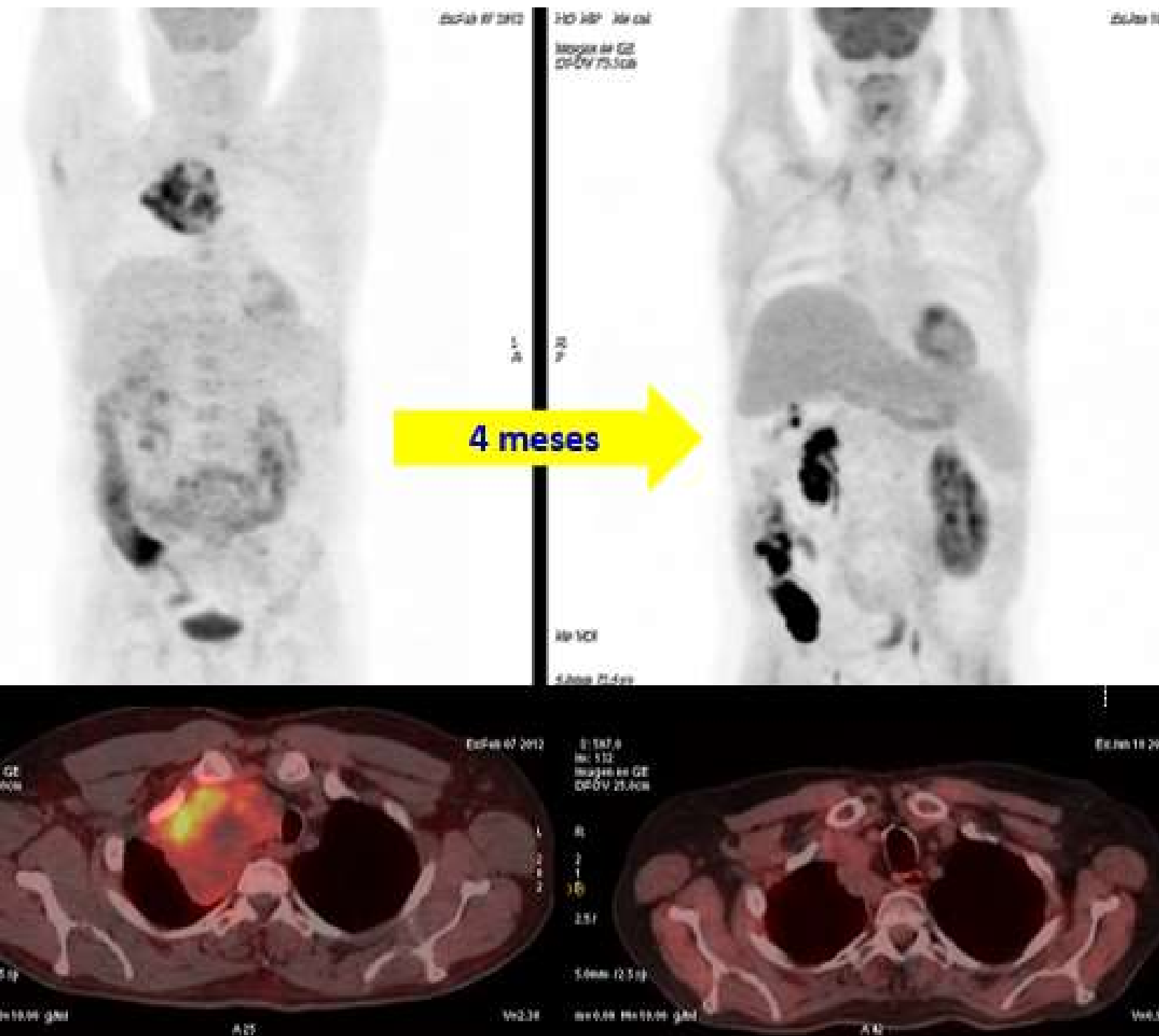
PERCIMT

Criterios HOPKINS

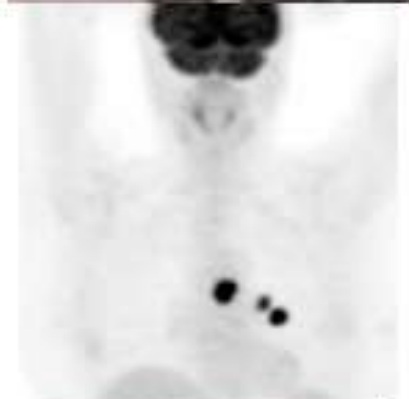
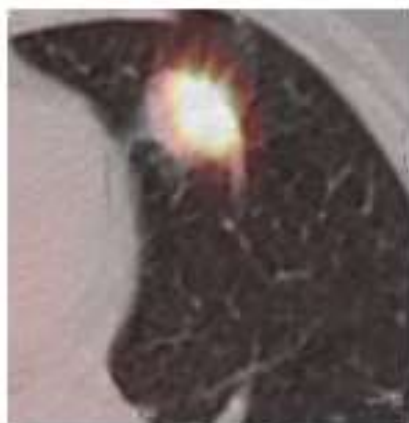
| | | |
|---|---|--|
| - | 1 | Captación focal en el tumor primario y las adenopatías menor que el pool vascular |
| - | 2 | Captación focal en el tumor primario y las adenopatías mayor que el pool vascular |
| - | 3 | Captación difusa en el tumor primario o las adenopatías, mayor que la captación hepática |
| + | 4 | Captación focal en el tumor primario o las adenopatías mayor que la captación hepática |
| + | 5 | Captación focal e intensa de FDG en el tumor primario y las adenopatías |

Tumores ORL, pulmón y páncreas

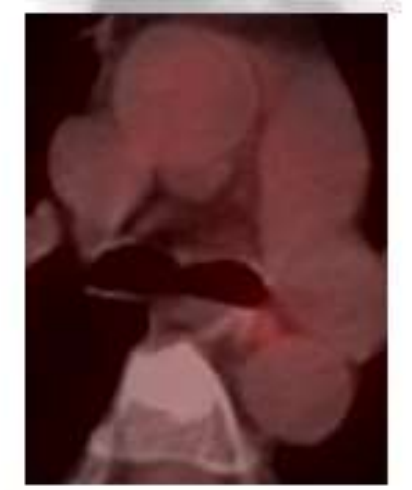
RESPUESTA COMPLETA



RESPUESTA COMPLETA

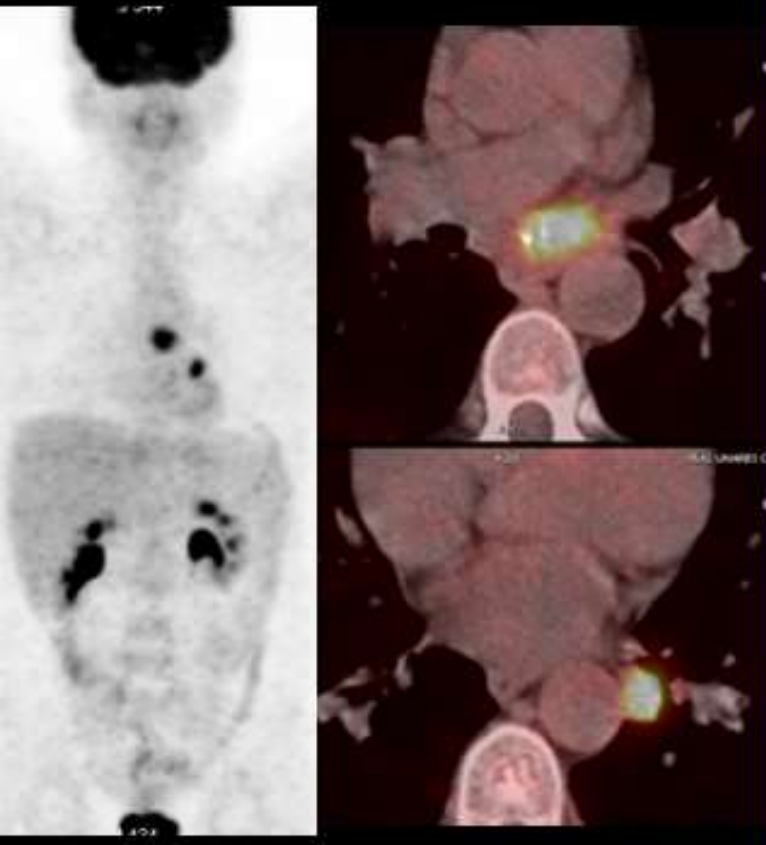


5 meses

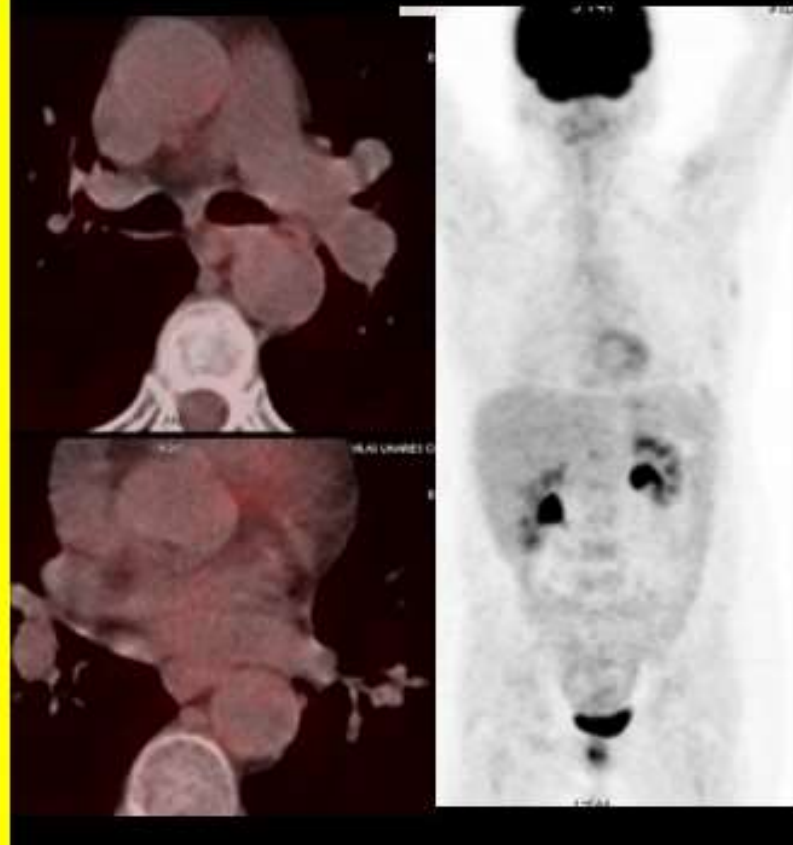


RESPUESTA COMPLETA

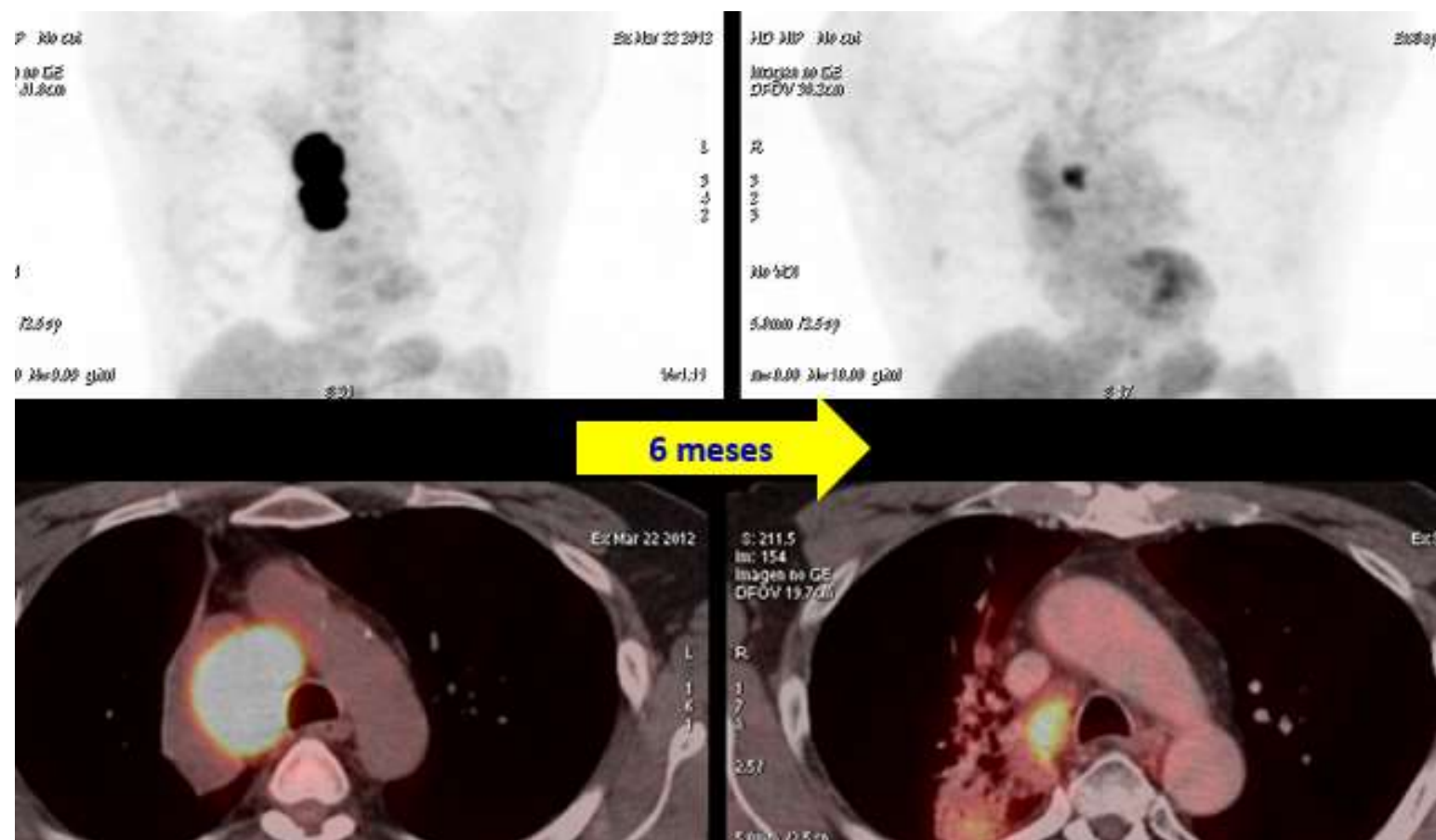
22 marzo 2012



27 agosto 2012



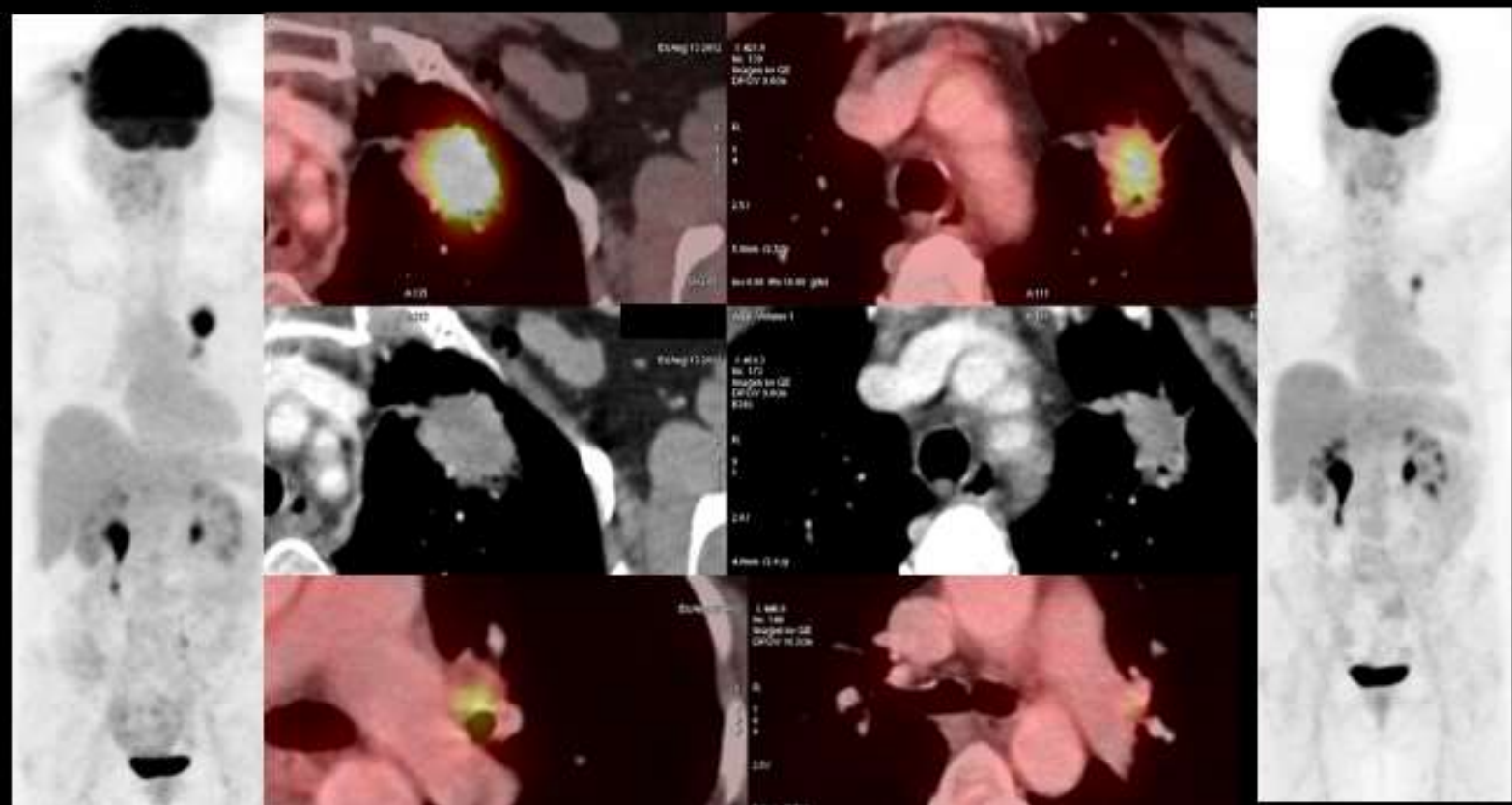
RESPUESTA PARCIAL



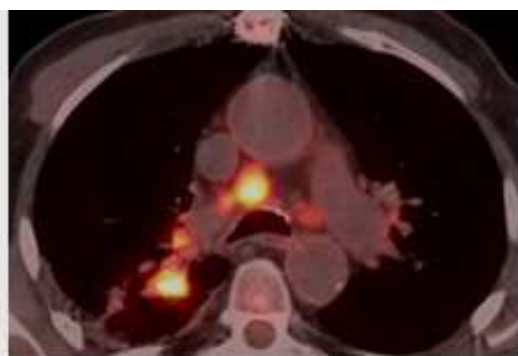
RESPUESTA PARCIAL

13/8/12

10/10/12

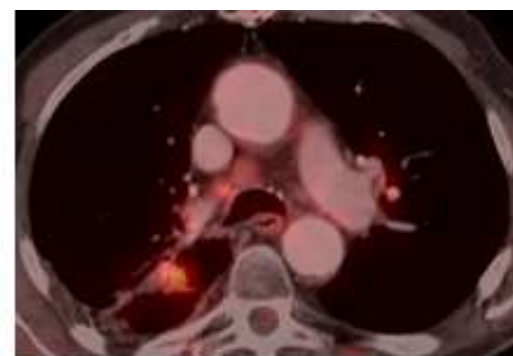


RESPUESTA PARCIAL



Respuesta parcial de la lesión pulmonar derecha.

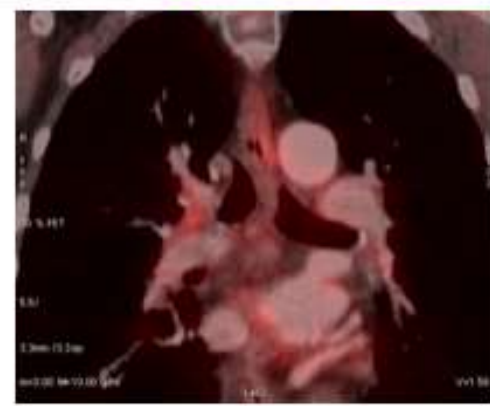
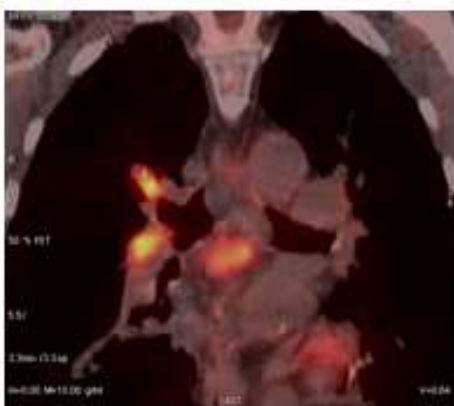
Importante respuesta de la afectación ganglionar



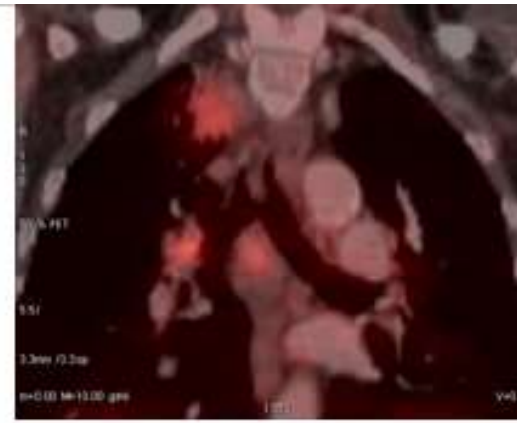
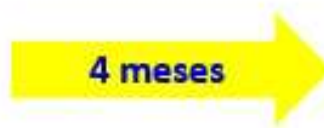
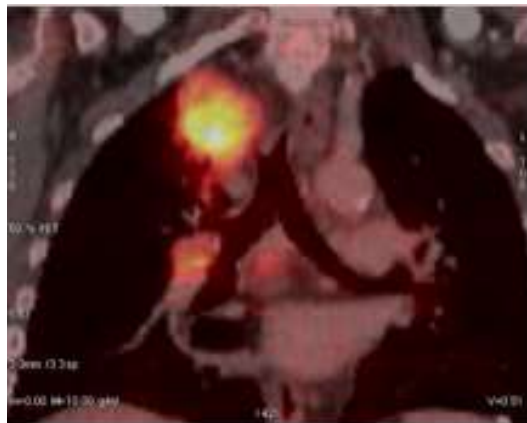
Findings

■ PD: Progressive disease
 ■ SD: Stable disease
 ■ PR: Partial response
 ■ CR: Complete response

| Lesion | SUV Max [SUVbw g/ml] | | TLG [SUVbw g] | |
|--------|----------------------|------------|---------------|------------|
| | 2010-01-12 | 2010-03-02 | 2010-01-12 | 2010-03-02 |
| 1 | 11.9 | 2.7 | 30.2 | 1.9 |
| 2 | 12.4 | - | 78.9 | - |
| 3 | 12.2 | 2.9 | 58.0 | 1.3 |
| 4 | 6.5 | - | 38.3 | - |
| 5 | 4.6 | 5.2 | 8.1 | 6.0 |



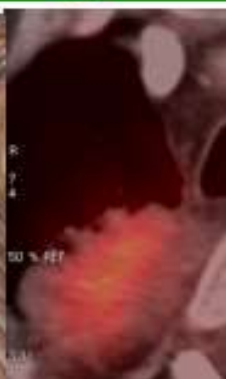
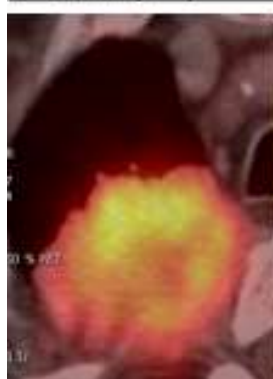
RESPUESTA PARCIAL



Findings

■ PD: Progressive disease
 ■ SD: Stable disease
 ■ PR: Partial response
 ■ CR: Complete response

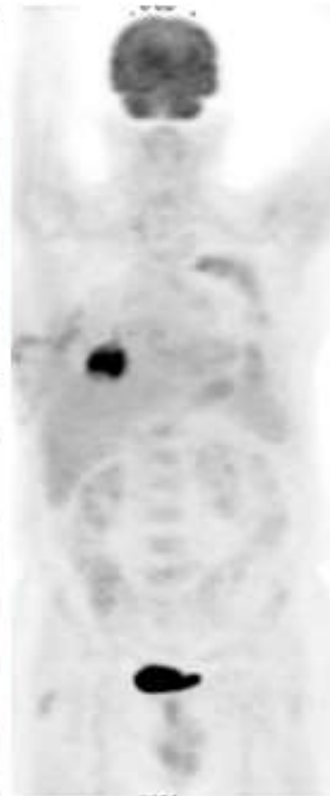
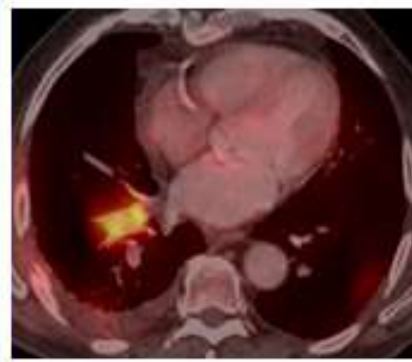
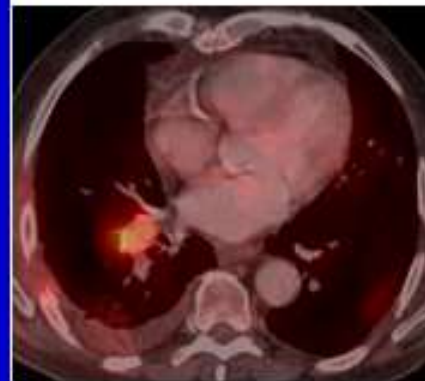
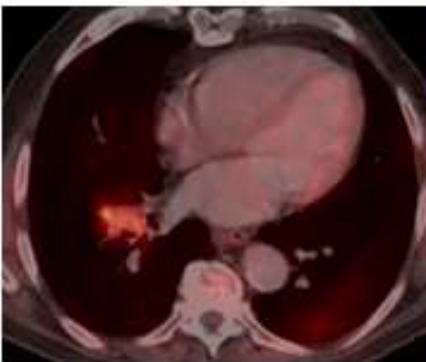
| Lesion | SUV Max [SUVbw g/ml] | | TLG [SUVbw g] | |
|---------|----------------------|------------|---------------|------------|
| | 2010-02-25 | 2010-06-01 | 2010-02-25 | 2010-06-01 |
| 1 | 14.0 | 5.3 | 417.7 | 88.7 |
| 2 | 5.9 | 5.1 | 31.5 | 7.6 |
| Summary | 14.0 | 5.3 | 449.1 | 96.3 |



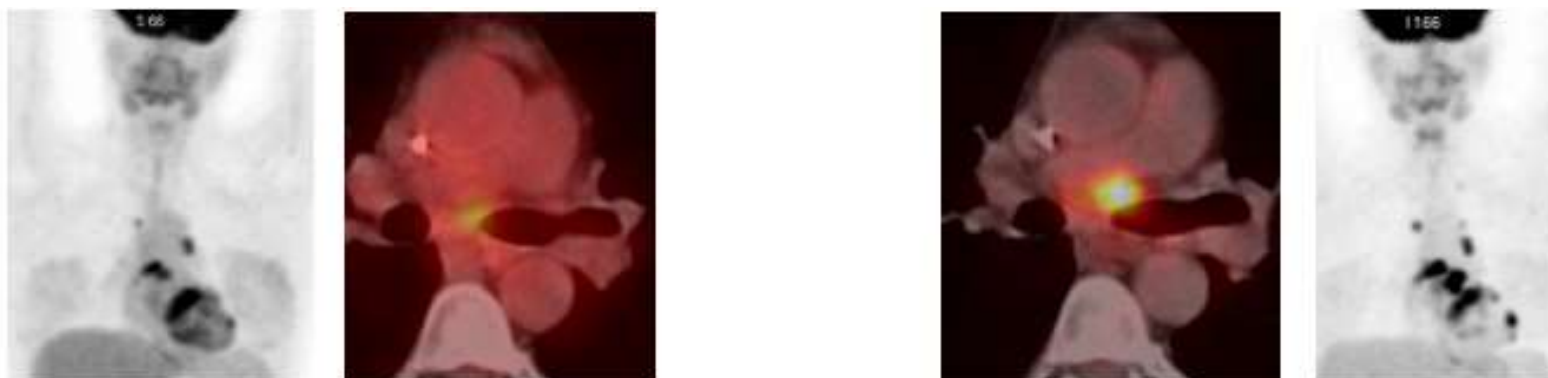
PROGRESION TUMORAL

Junio

Septiembre



PROGRESION TUMORAL



Findings

■ PD: Progressive disease
 ■ SD: Stable disease
 ■ PR: Partial response
 ■ CR: Complete response

| Lesion | SUV Max [SUVbw g/ml] | | | TLG [SUVbw g] | | |
|--------|----------------------|------------|------------|---------------|------------|------------|
| | 2010-04-29 | 2010-09-20 | 2011-01-10 | 2010-04-29 | 2010-09-20 | 2011-01-10 |
| 1 | 15.5 | 14.0 | 11.3 | 651.1 | 782.4 | 1,102.2 |
| 2 | 4.1 | 3.9 | 3.5 | 9.4 | 10.7 | 11.3 |
| 3 | 8.0 | 11.6 | 5.8 | 916.0 | 650.8 | 978.8 |

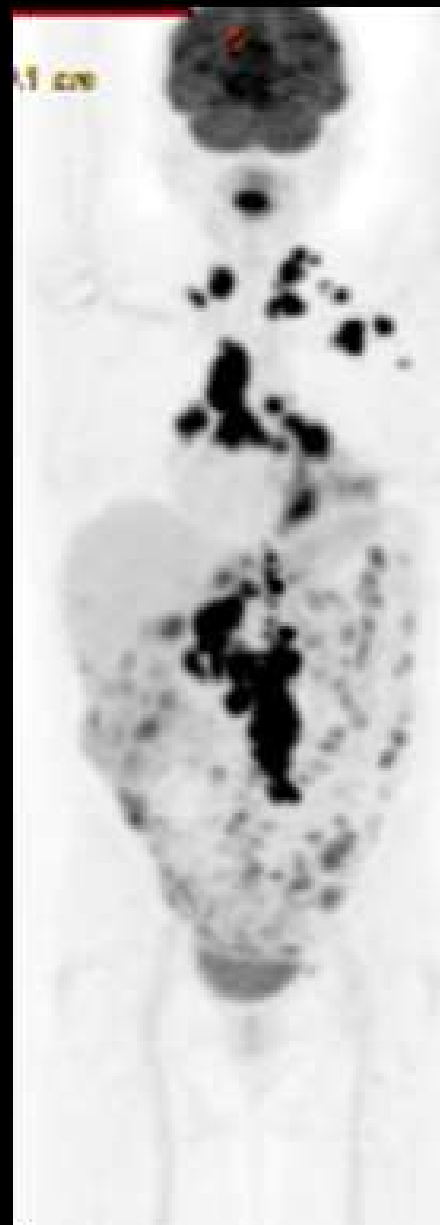


4 meses



PROGRESION TUMORAL

Carcinoma de ovario estadio IV



PROGRESION TUMORAL

Carcinoma epidermoide del reborde alveolar

