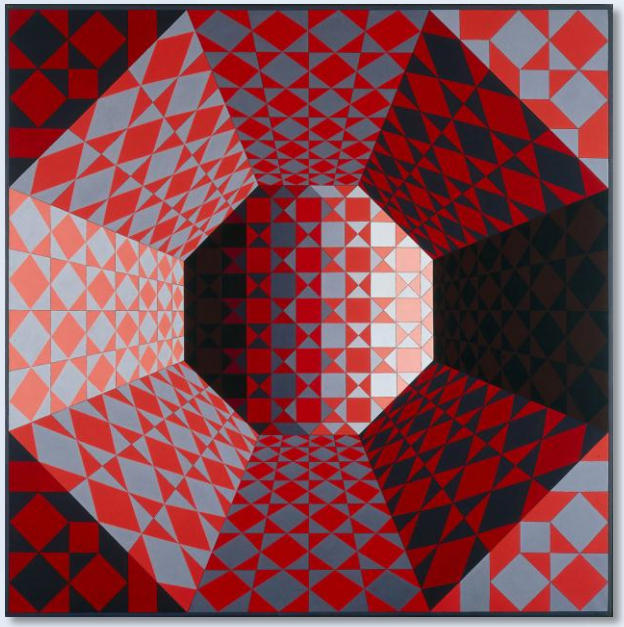

Can FDG-PET help individualize the treatment of colorectal cancer patients ?

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Institut Jules Bordet – Brussels
01/10/2012

Institut Jules Bordet

VIENNA 2012 ESMO congress

www.esmo2012.org

Disclosure slide

No conflict of interest

to declare in relation to this topic

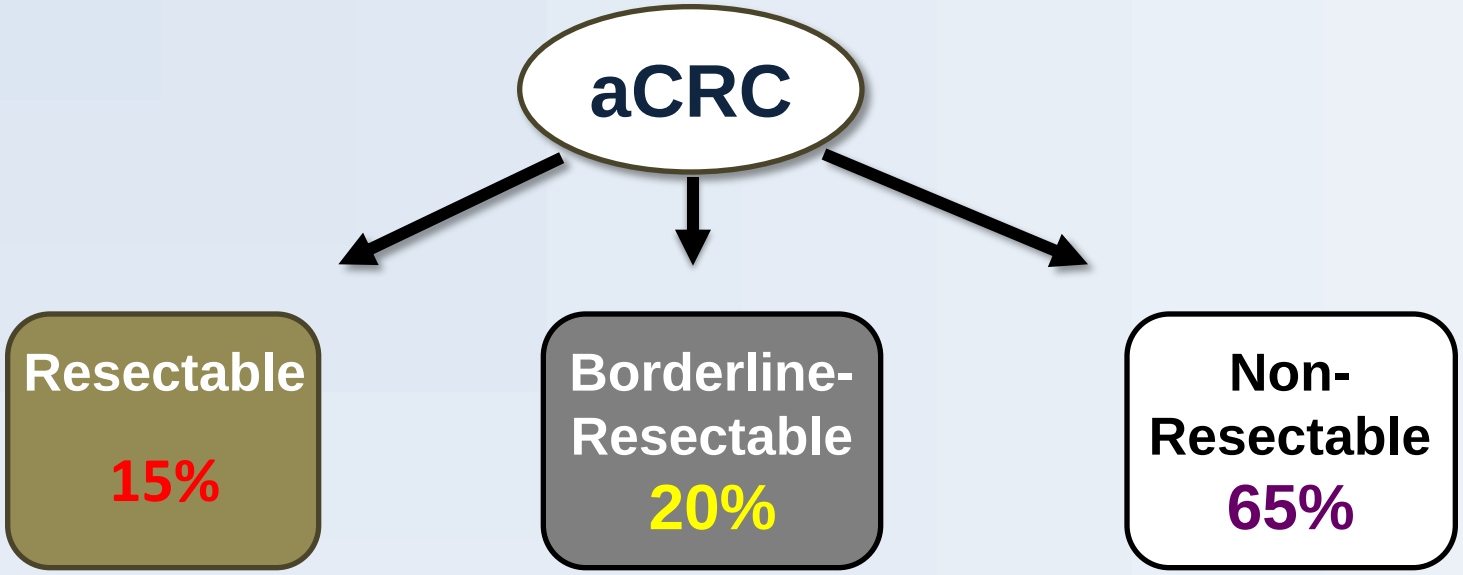
« None of the arts theorizes about individual cases.
Medicine, for instance, does not theorize about what will help to cure Socrates or Callias, but only about what will help to cure any or all of a given class of patients… : individuals are so infinitely various that no systematic knowledge of them is possible. »

Aristotle, Rhetoric, Book I, Chapter 2:1356b

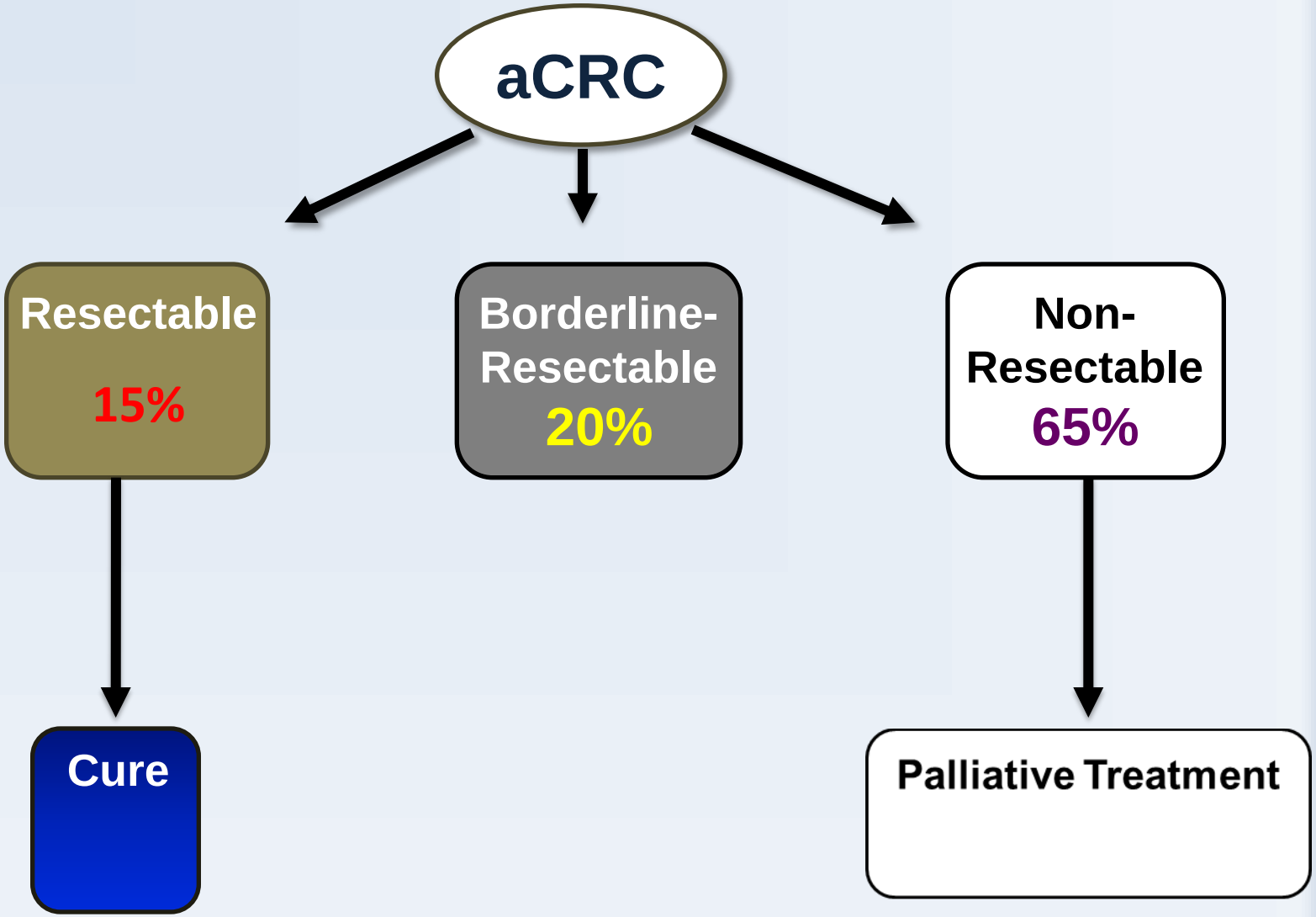
Treating a patient means

1. **Choosing a strategy** that fits
    - to the patient
    - to the disease
    - to the perception we have of the clinical situation
2. **Choosing a treatment** (drug(s) or not) that fits to the strategy
3. **Reassess** the adequation of both strategy and treatment

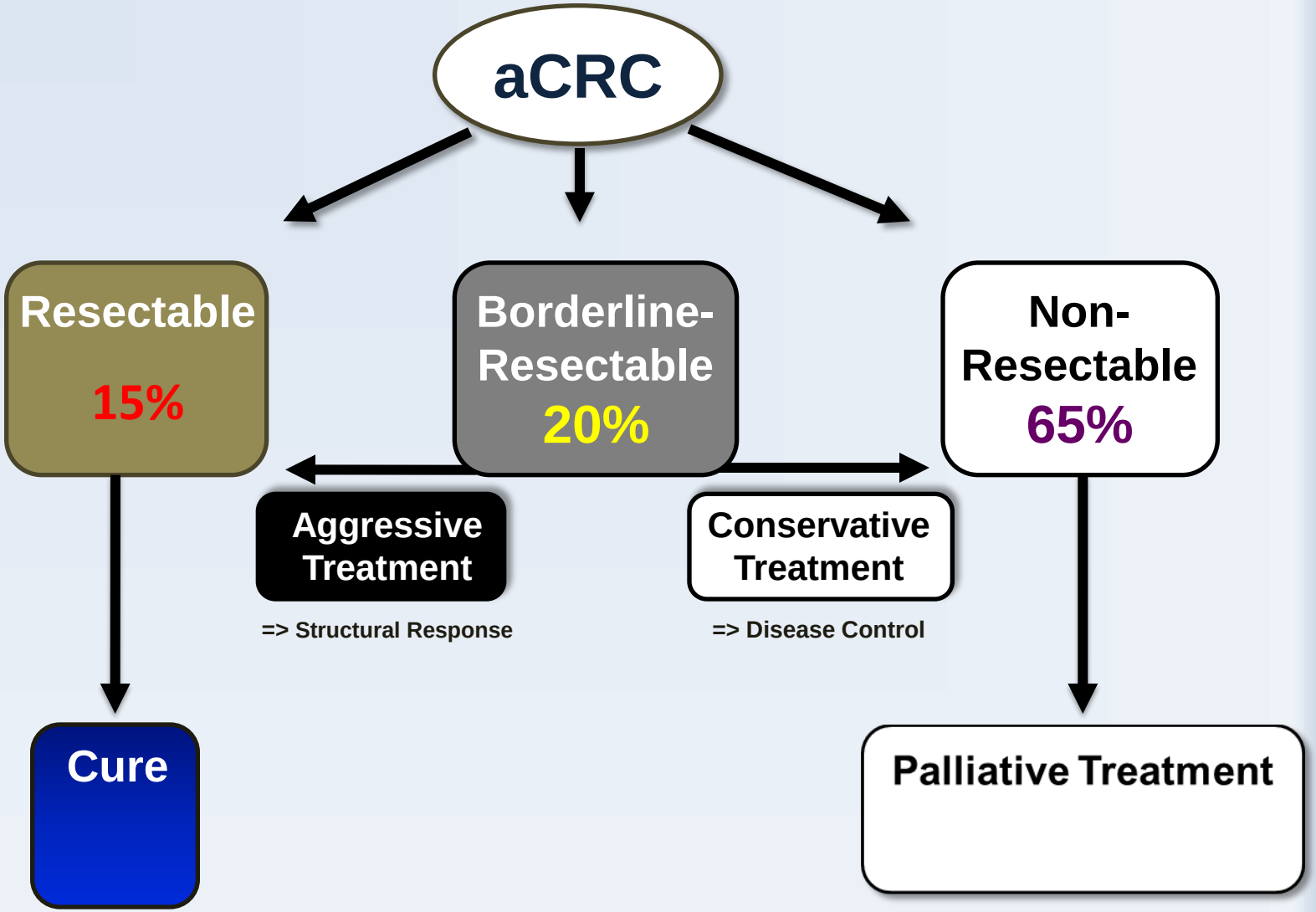
aCRC : Choosing a Strategy



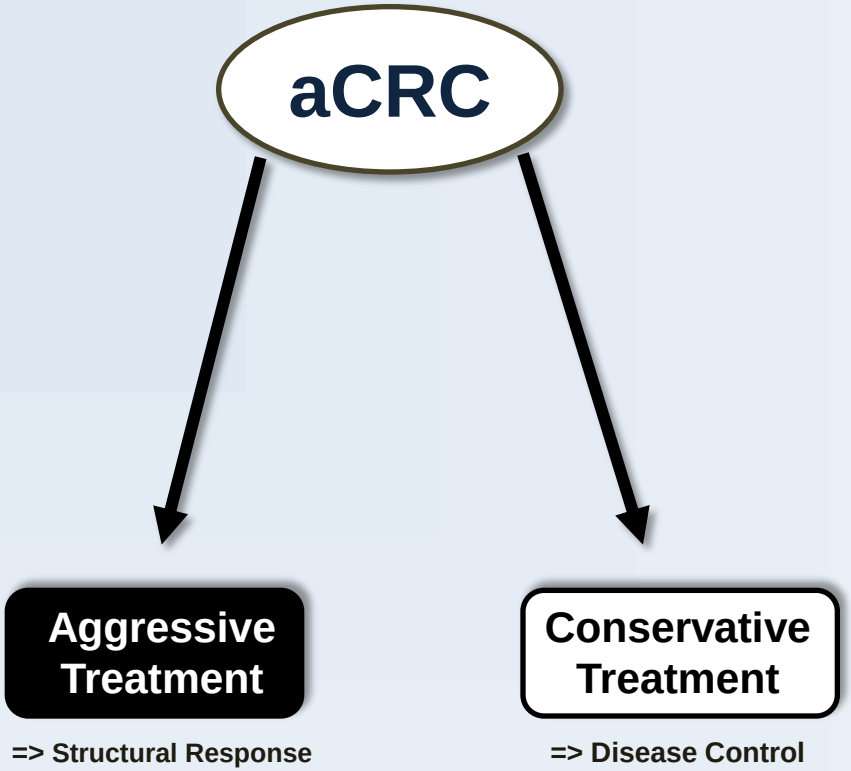
aCRC : Choosing a Strategy



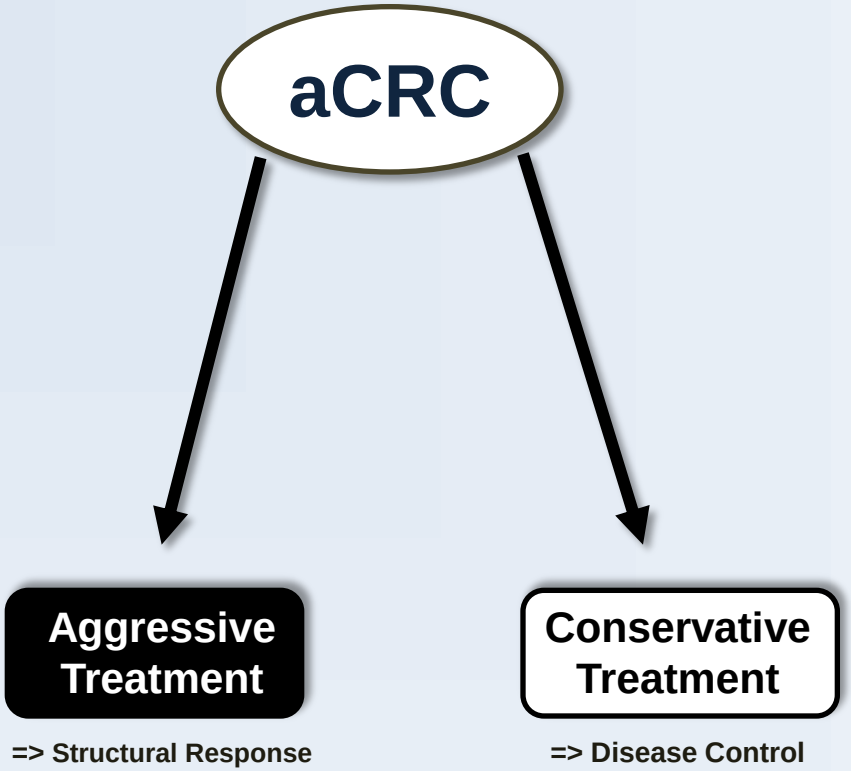
aCRC : Choosing a Strategy



aCRC : Choosing a Strategy



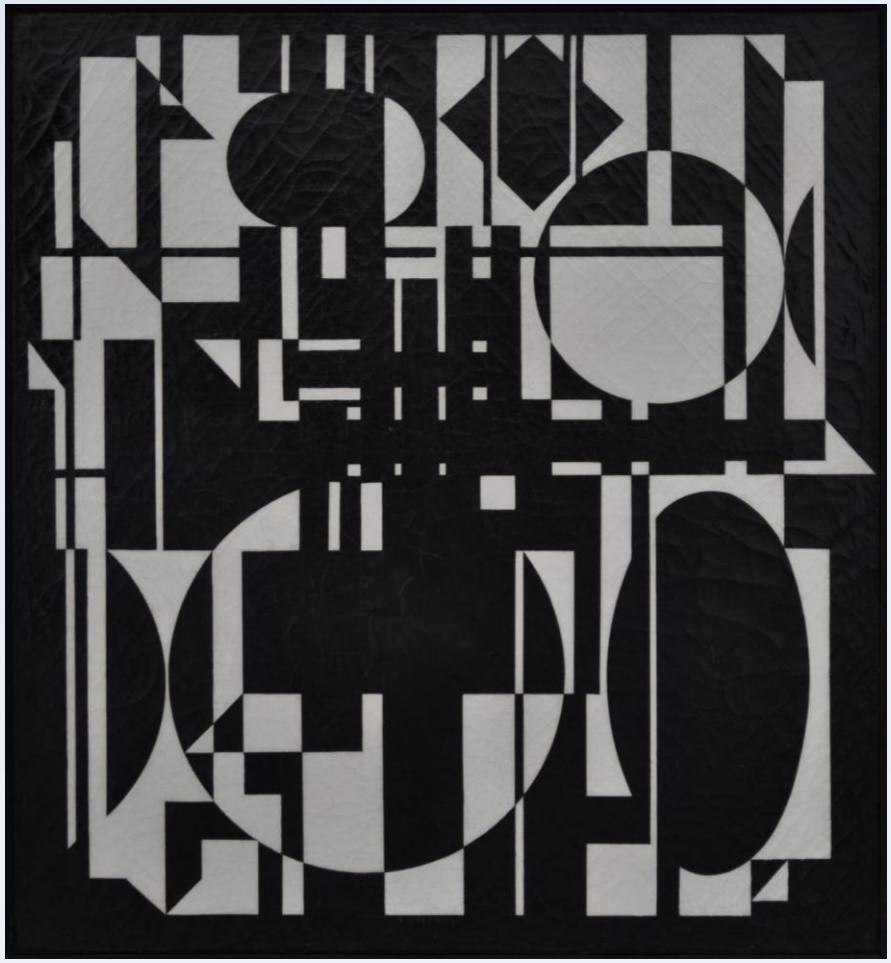
aCRC : Choosing a Strategy



- change therapy before it's too late
- change strategy because it's too late
- avoid useless toxicity

Identify quickly non-responders with highest possible NPV*

Choosing and assessing the treatment



Validated Tools used to assess anticancer treatment (in CLINICAL STUDIES)

- Overall Survival
- Progression-Free Survival
- Quality of Life
- Symptoms
- Response Rate

Discrepancy between daily practice and clinical trial setting about treatment outcome assessment

Tool	Accuracy for Clinicians	Accuracy for Clinical Trials	Quickly available
Overall Survival	no	yes	no
Progression-Free Survival	no	yes	no
Quality of Life	no	+/-	no
Symptoms	+/-	+/-	no
Response rate	yes	yes	yes

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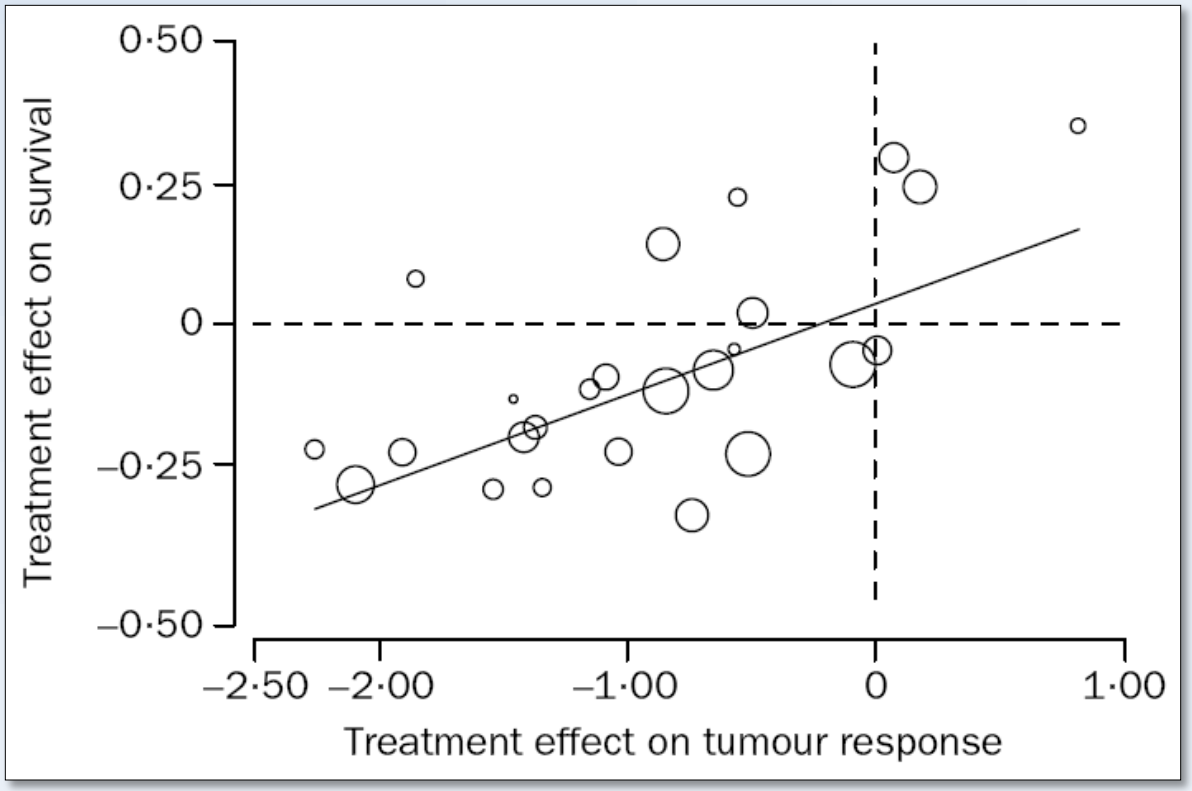
Correlation between response rate and overall survival



Response is correlated to Overall Survival , but

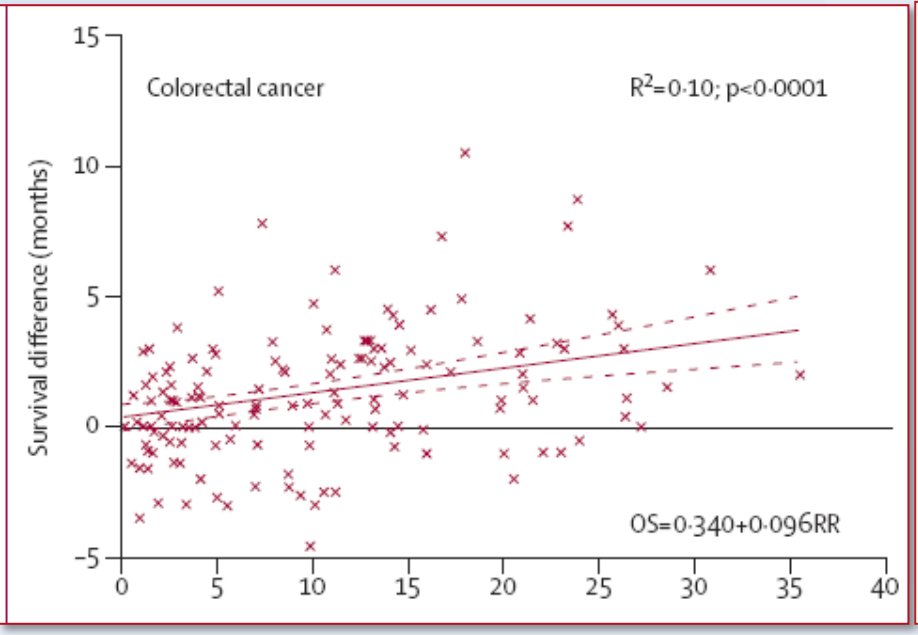
POORLY

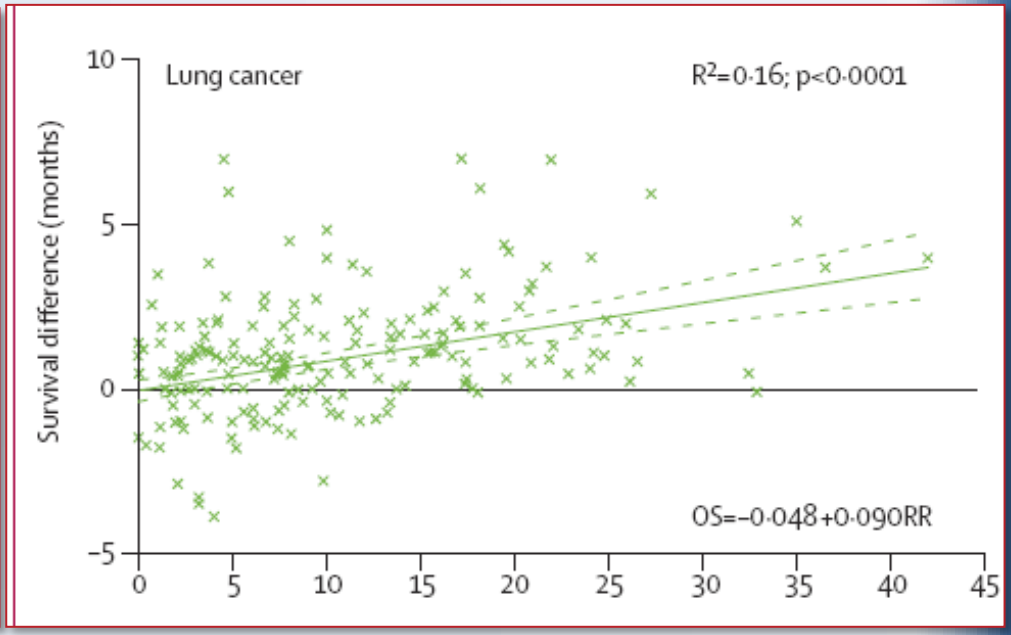
(<50% survival benefit might be explained by response variability)

Coefficient of determination of the regression line is 0.38 (0.09-0.68)

Buyse et al Lancet 2000

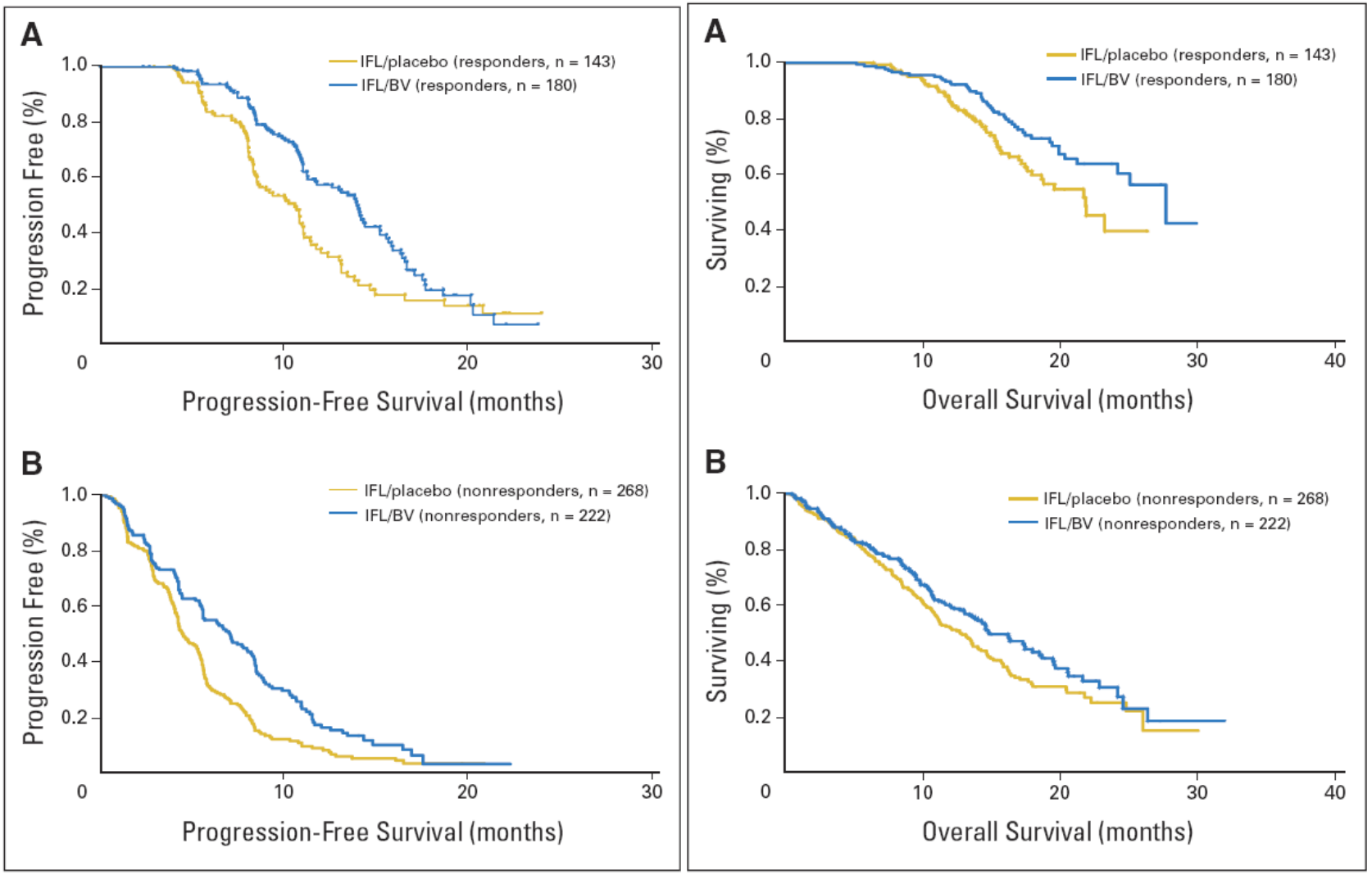
Correlation between response rate and overall survival





Johnson et al, Lancet Oncology 2006

New drugs :
Structural changes not always reflect clinical benefit



Grothey JCO 2008

Why?

Pitfalls of response assessment

A. **Technical issues**
   1. Assumption of spherical tumor growth
   2. Tumoral heterogeneity
   3. Clinical benefit independant from structural response

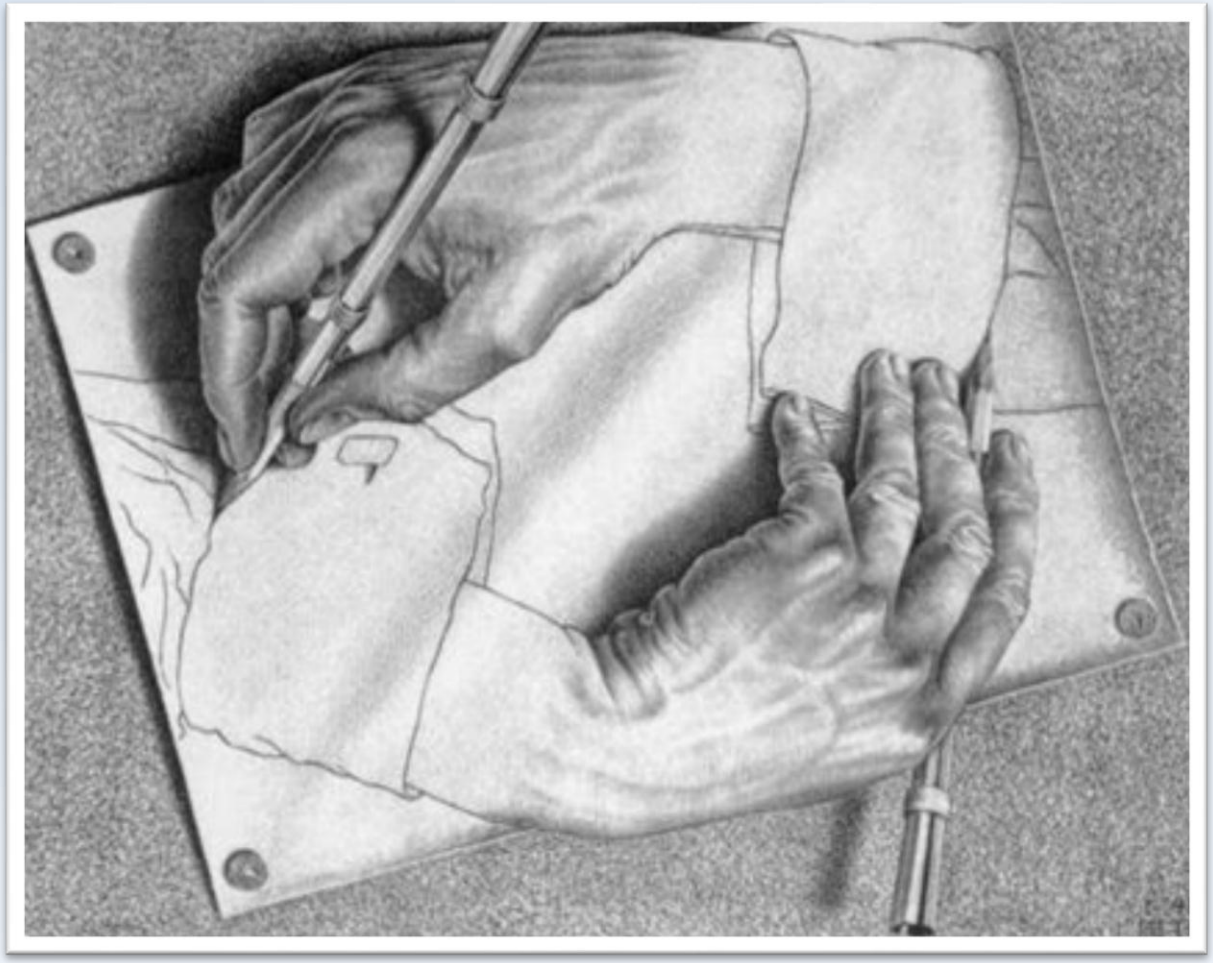
B. **Methodological Issues**
   1. Central review impact
   2. Sample size impact

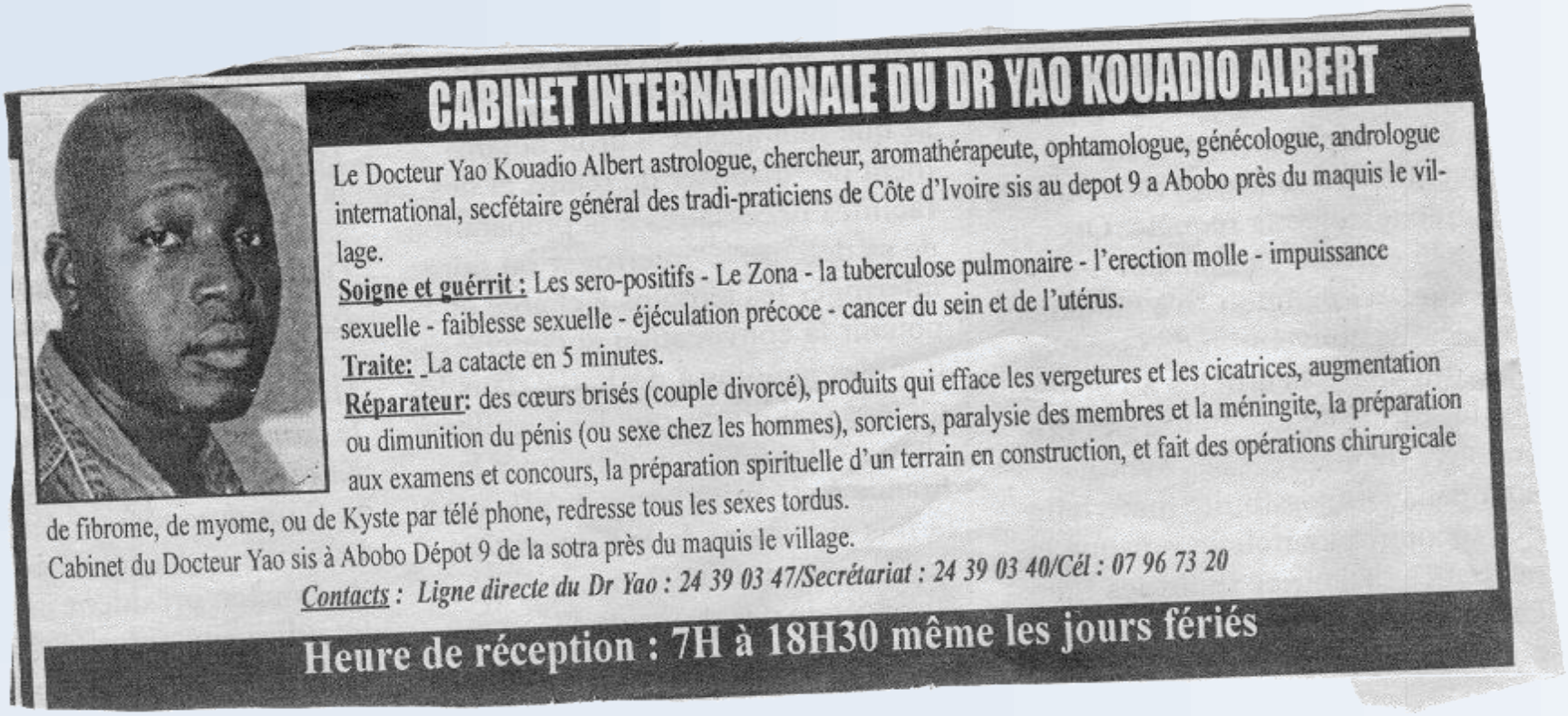
C. **Philosophical issues**

Structural (radiological) response assessment

1. Is the fastest way to assess treatment benefit
   - ✓ in daily practice
   - ✓ in clinical trials
2. But :
   a. Too late (6-8 weeks between assessments)
   b. Poorly correlated to survival

New assessment tools





CABINET INTERNATIONALE DU DR YAO KOUADIO ALBERT

Le Docteur Yao Kouadio Albert astrologue, chercheur, aromathérapeute, ophtamologue, génécologue, andrologue international, secfétaire général des tradi-praticiens de Côte d'Ivoire sis au depot 9 a Abobo près du maquis le village.

Soigne et guérrit : Les sero-positifs - Le Zona - la tuberculose pulmonaire - l'erection molle - impuissance sexuelle - faiblesse sexuelle - éjéculation précoce - cancer du sein et de l'utérus.

Traite: La catacte en 5 minutes.

Réparateur: des cœurs brisés (couple divorcé), produits qui efface les vergetures et les cicatrices, augmentation ou dimunition du pénis (ou sexe chez les hommes), sorciers, paralysie des membres et la méningite, la préparation aux examens et concours, la préparation spirituelle d'un terrain en construction, et fait des opérations chirurgicale de fibrome, de myome, ou de Kyste par télé phone, redresse tous les sexes tordus.

Cabinet du Docteur Yao sis à Abobo Dépot 9 de la sotra près du maquis le village.

Contacts : Ligne directe du Dr Yao : 24 39 03 47/Secrétariat : 24 39 03 40/Cél : 07 96 73 20

Heure de réception : 7H à 18H30 même les jours fériés

Predictive value :

- ✓ 100% **Sensitivity**
- ✓ 0% **Specificity**
- ✓ 50% **PPV**
- ✓ 0% **NPV**

Tumoral markers

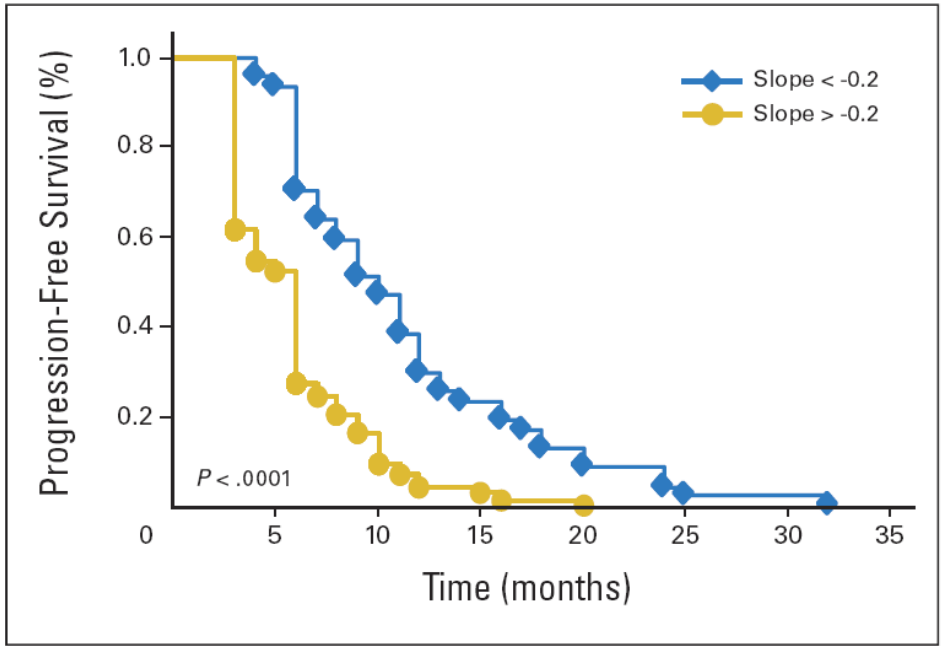


Fig 3. Progression-free survival for patients with carcinoembryonic antigen slopes less than −0.2 versus CEA slopes more than −0.2.

Predictive value :

- ✓ 74.5% **Sensitivity** (95% CI, 60.4-85.7%)
- ✓ 84.7% **Specificity** (95% CI, 74.3-92.1%)
- ✓ 77.6% **PPV** (95% CI, 74.6-80.6%)
- ✓ 82.4% **NPV** (95% CI, 80.4-84.4%)

Iwanicki-Caron J Clin Oncol 2008

Circulating Tumor Cells (CTC's)

Table 3. Response to Imaging *v* CTC Category at 3-5 Weeks

Response to Therapy by Imaging (RECIST criteria)	CTCs 3-5 Weeks After the Initiation of Therapy				Total	% of Total Set
	< 3 CTCs		≥ 3 CTCs			
	No.	%	No.	%		
Nonprogressive disease (stable disease, partial or complete response)	228	93	18	7	246	77
Progressive disease (or death)	54	73	20	27	74	23
Total	282	88	38	12	320	100

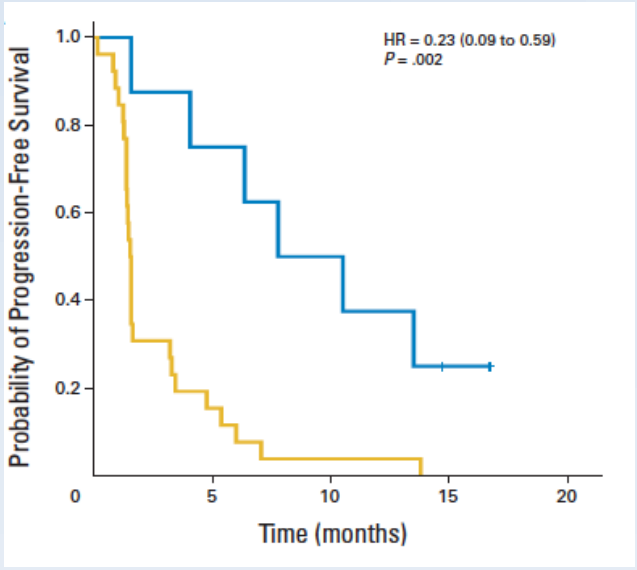
Abbreviations: CTC, circulating tumor cell; RECIST, Response Evaluation Criteria in Solid Tumors.

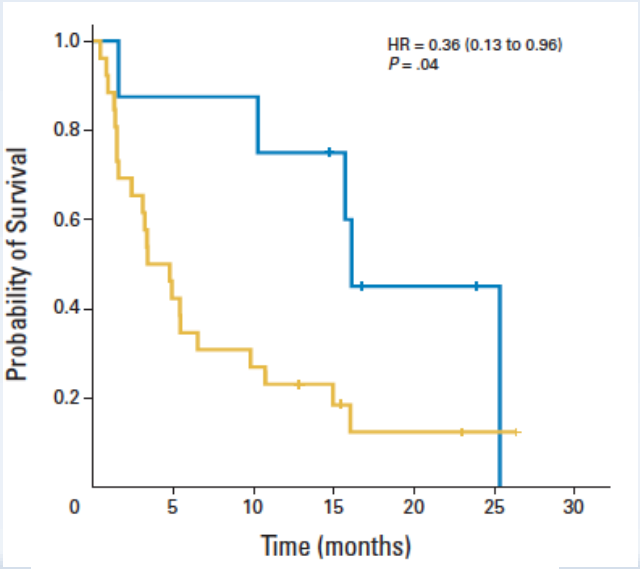
Predictive value :

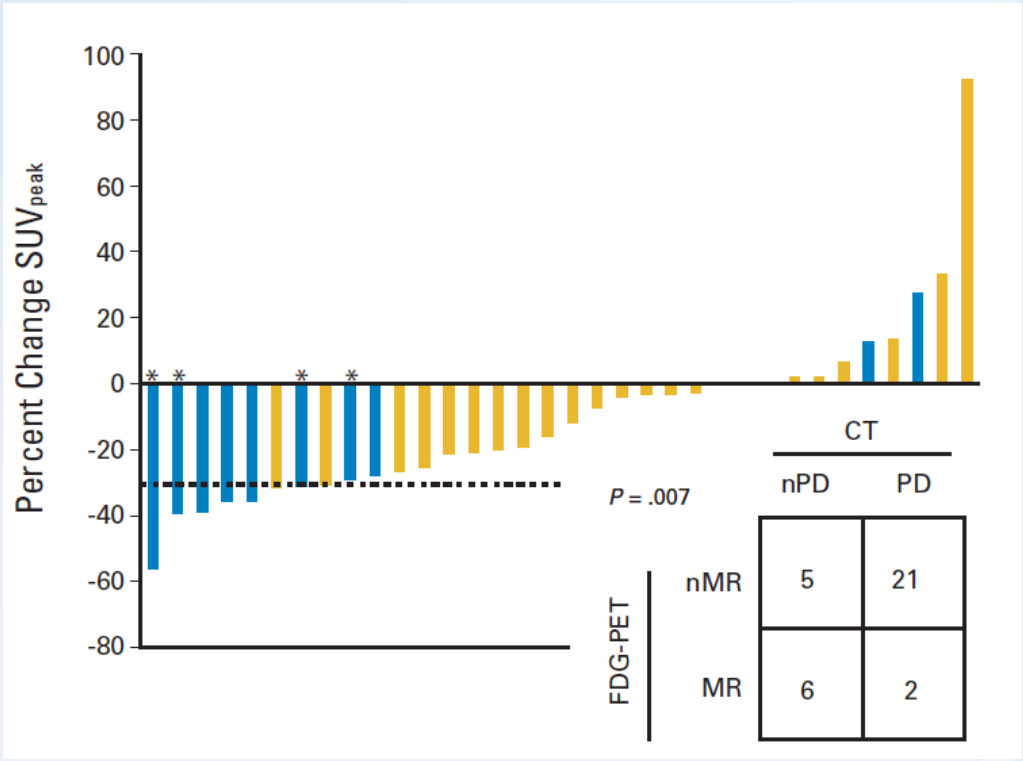
- ✓ 27% **Sensitivity** (95% CI, 17-39%)
- ✓ 93% **Specificity** (95% CI, 89-96%)
- ✓ 53% **PPV** (95% CI, 36-69%)
- ✓ 81% **NPV** (95% CI, 76%-85%)

Cohen, J Clin Oncol 2008

FDG-PET metabolic assessment : NSCLC treated with Erlotinib







Zander, J Clin Oncol 2011

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FDG-PET metabolic assessment : Esophageal adenocarcinoma

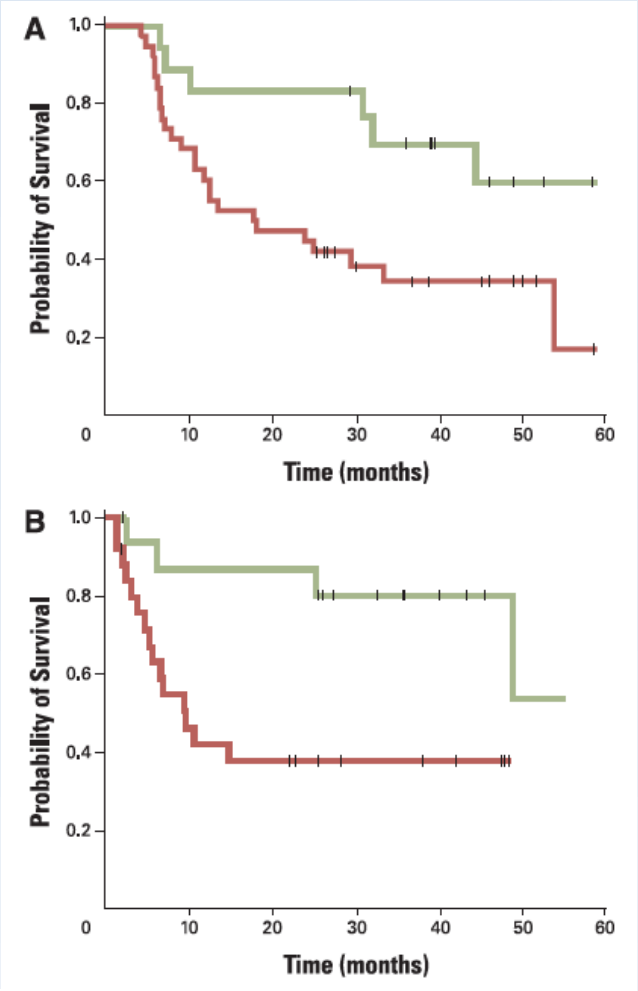


Table 3. Accuracy of Early Metabolic Response Evaluation

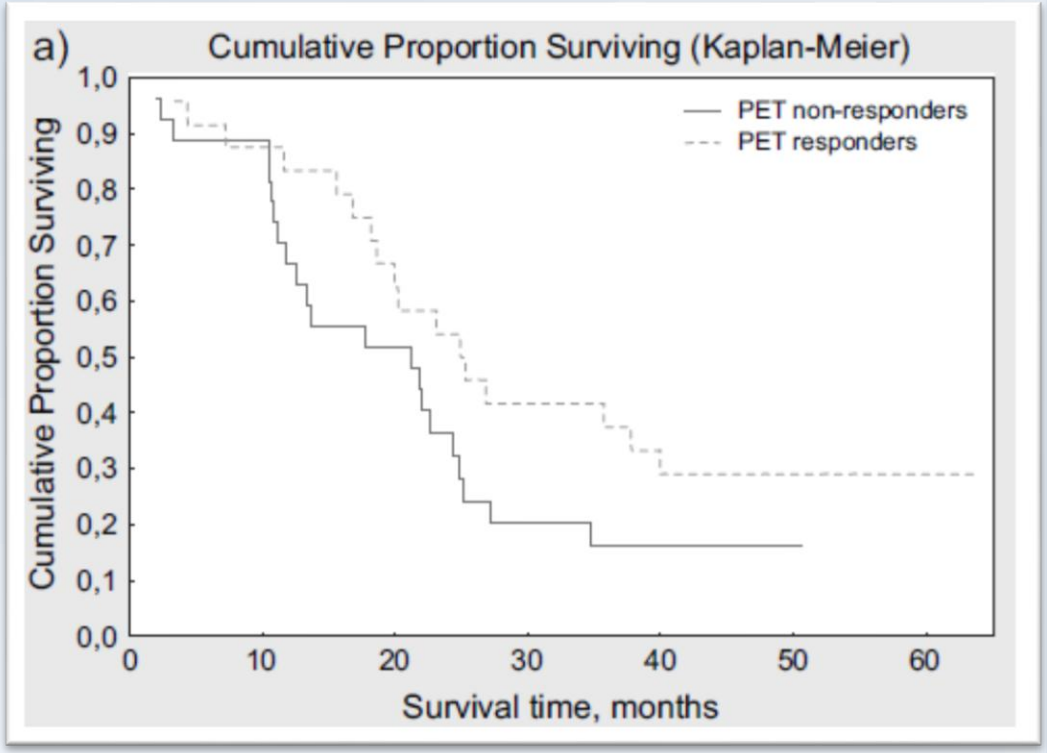
	Histopathologic Response		Clinical Response	
	No.	%	No.	%
Positive predictive value	8/18	44	14/18	78
Sensitivity	8/10	80	14/19	74
Negative predictive value	36/38	95	33/38	87
Specificity	36/46	78	33/37	89
Accuracy	44/56	79	47/56	84

Ott, J Clin Oncol 2006

FDG-PET metabolic assessment

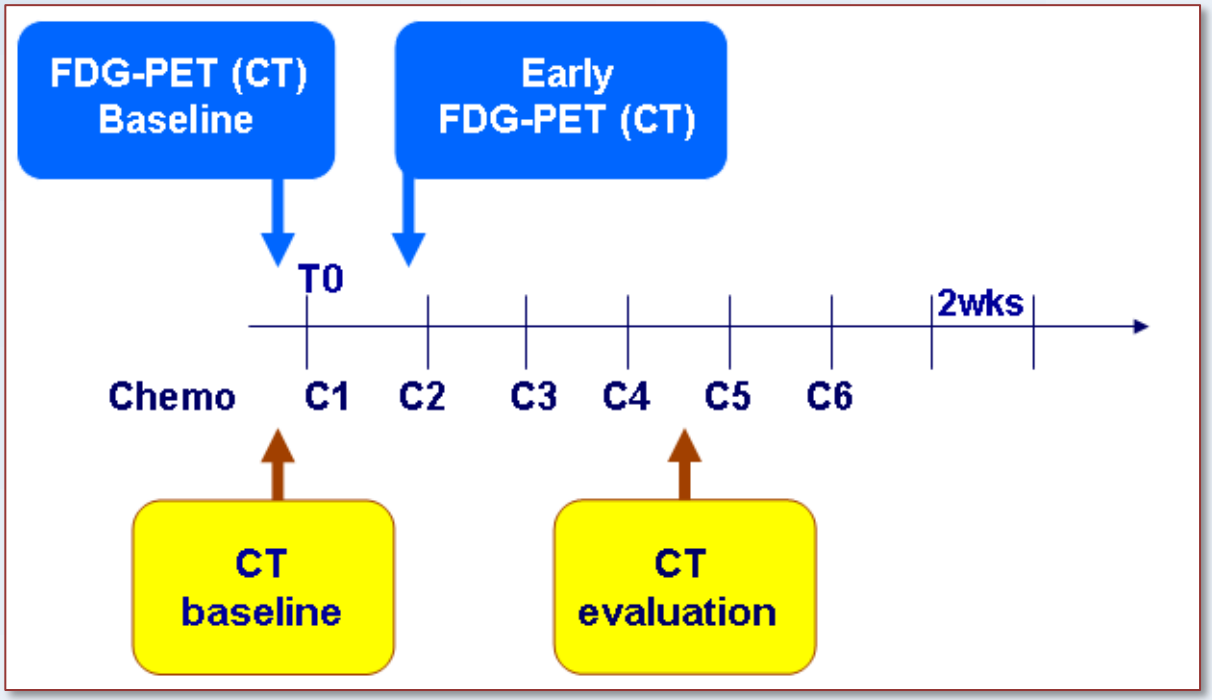
- ✓ **Sensitivity 77%**
- ✓ **Specificity 76%**
- ✓ **PPV 71%**
- ✓ **NPV 81%**
- ✓ **Non correlated with OS & TTP !**

RECIST-type assessment



Byström, Ann Oncol 2009

Early metabolic response assessment : the IJB experience



Hendlisz et al, Ann Oncol 2011

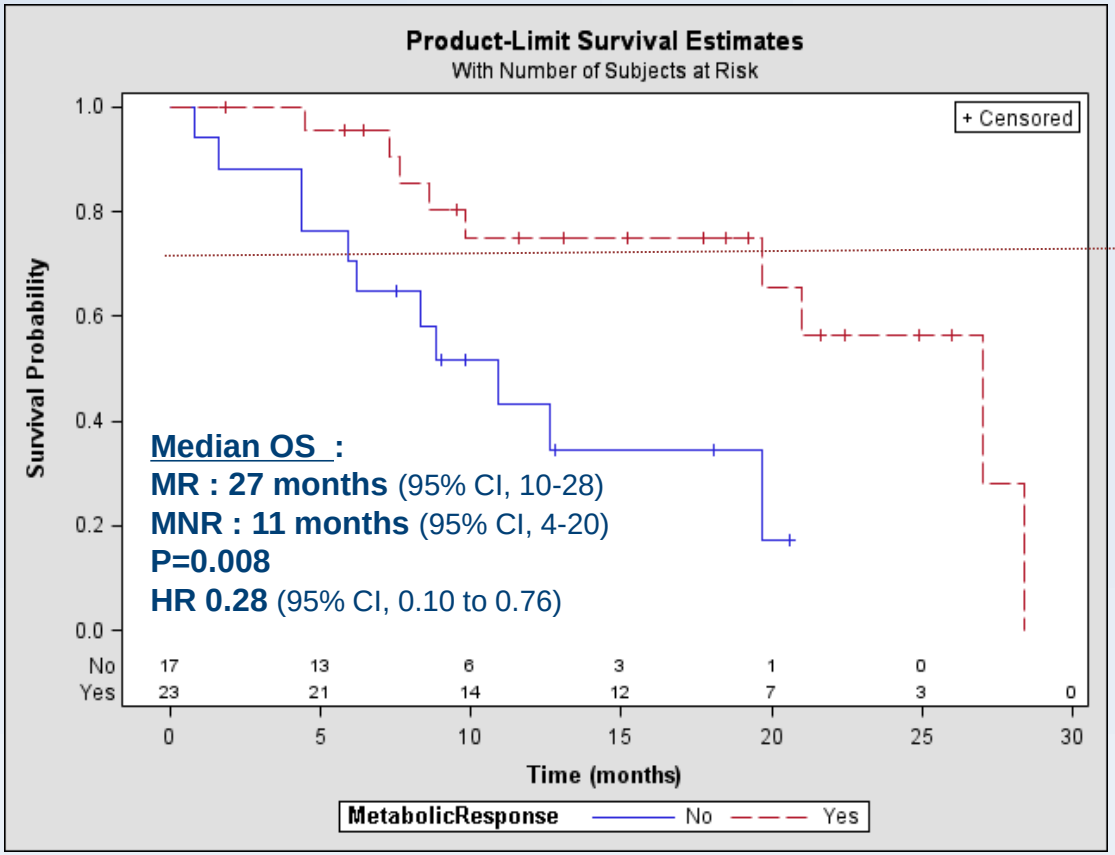
Early metabolic response assessment : the IJB experience

68% heterogeneity in metabolic response

Metabolic Response	
Class I	All lesions respond
Class II	Majority respond- No progressive lesion
Class III	Minority respond- No progressive lesion
Class IV	No lesion respond **or** At least 1 progressive lesion

Hendlisz et al, Ann Oncol 2011

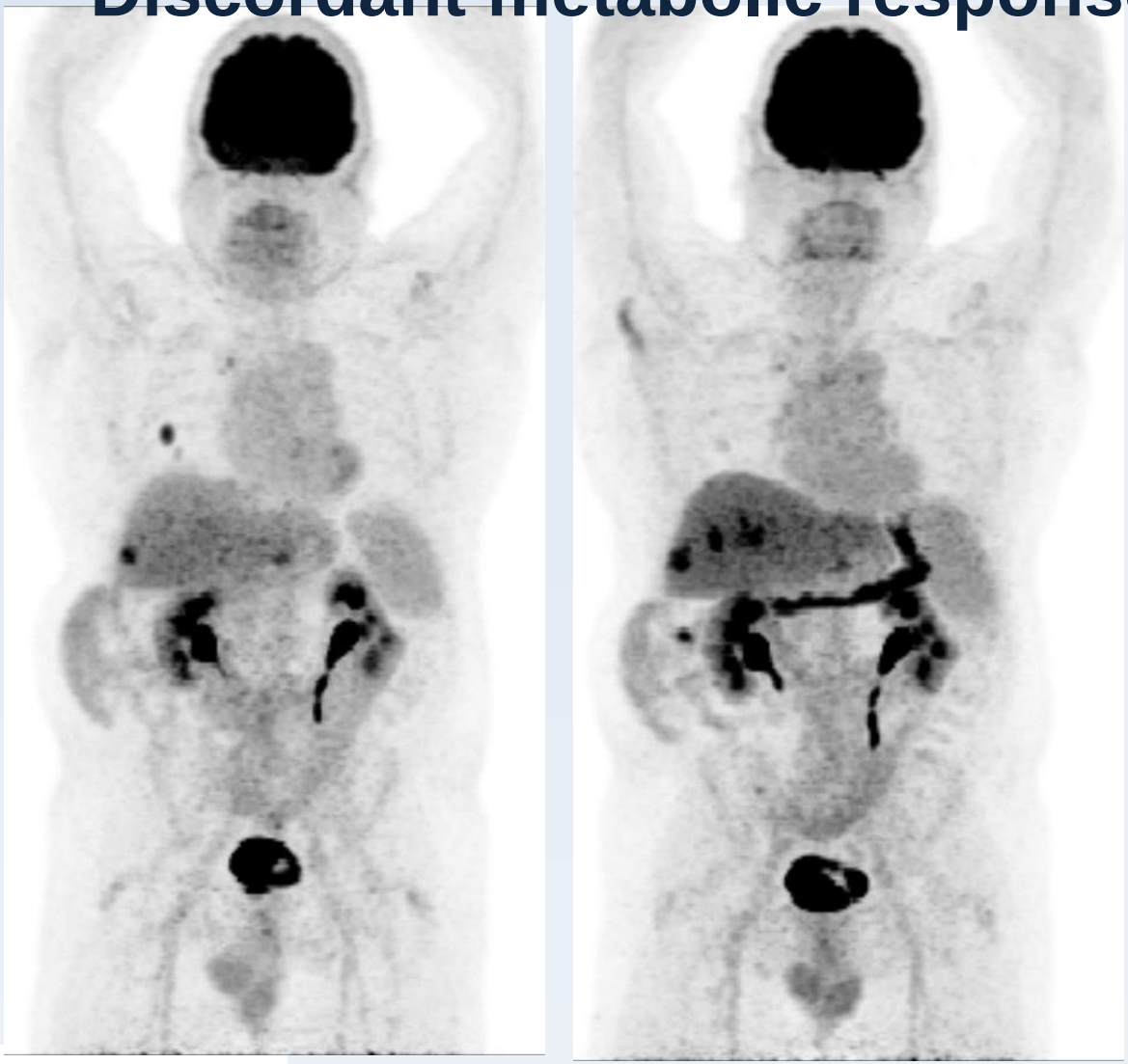
Early metabolic response assessment : the IJB experience



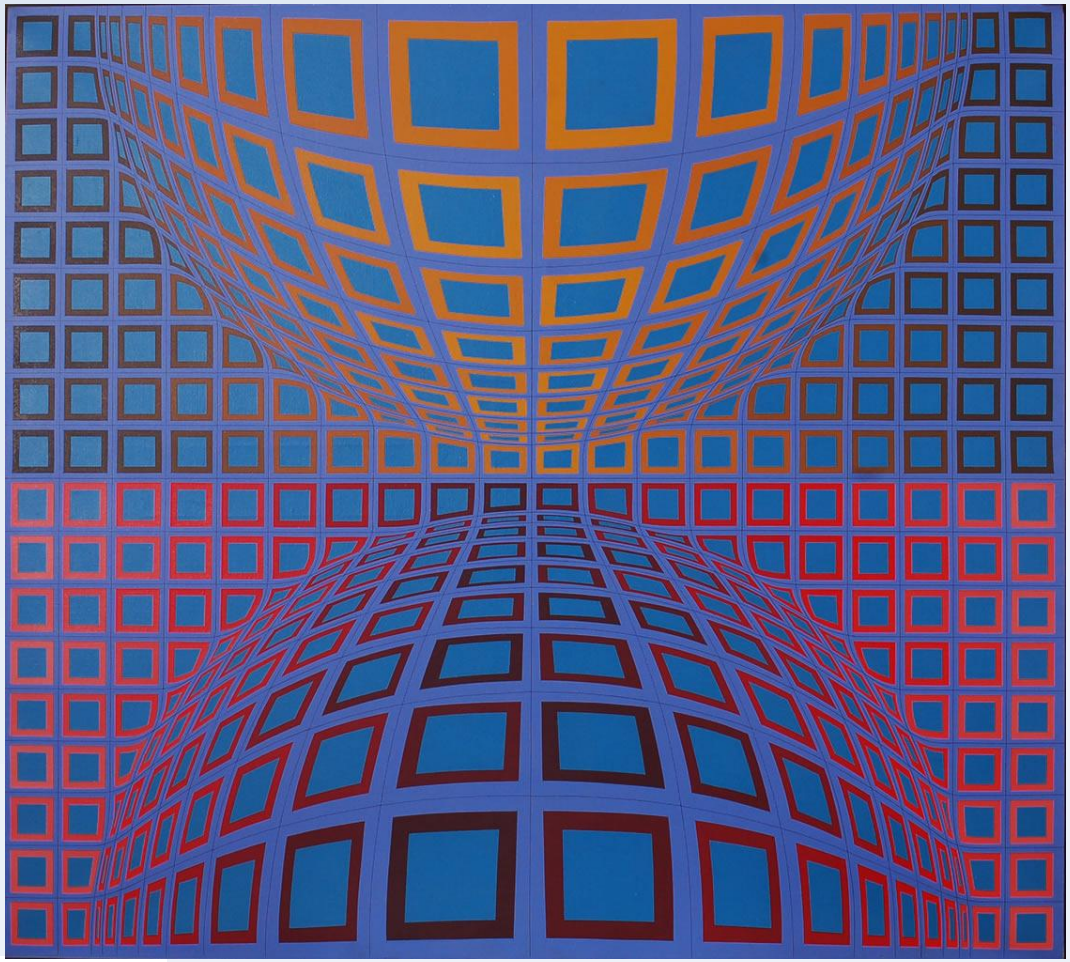
100%	**Sensitivity** (95%CI 69-100)
57%	**Specificity** (95%CI 37-75)
43%	**PPV** (95%CI 23-66)
100%	**NPV** (95%CI 80-100)

Hendlisz et al, Ann Oncol 2011

Early metabolic response assessment : Discordant metabolic response

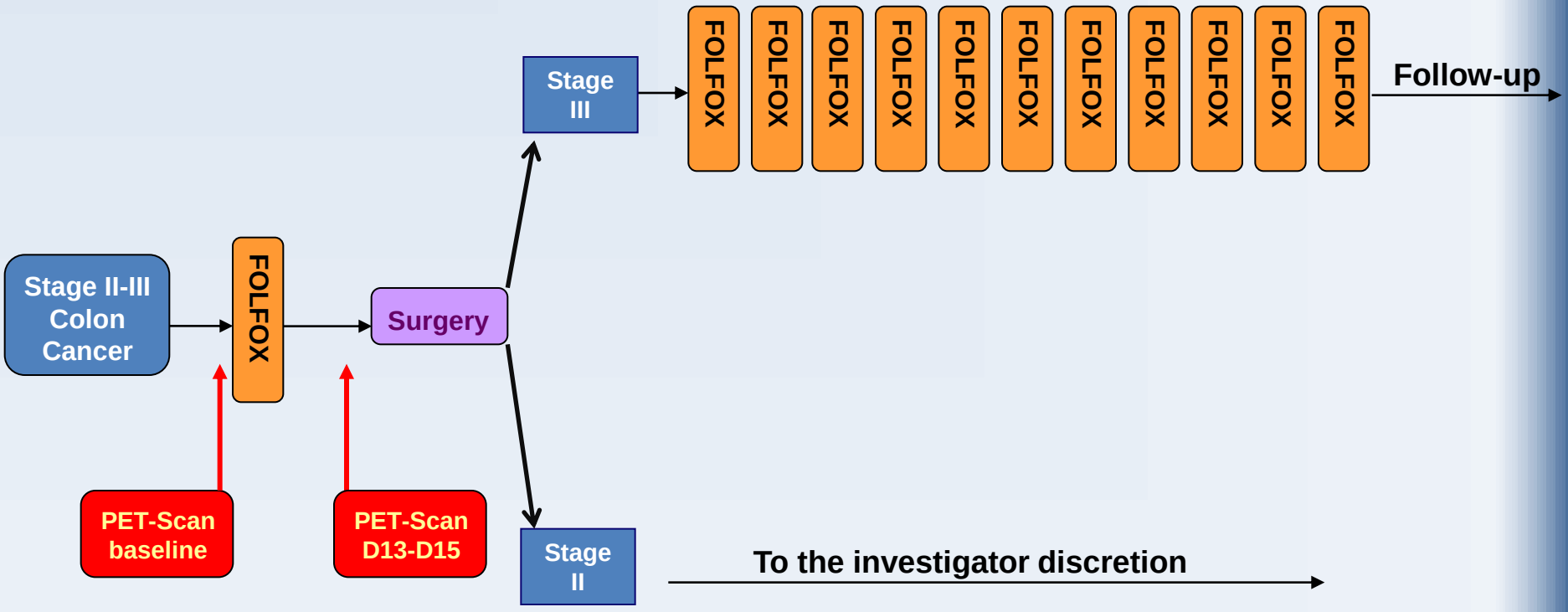


How could we use those faster and more precise tools?

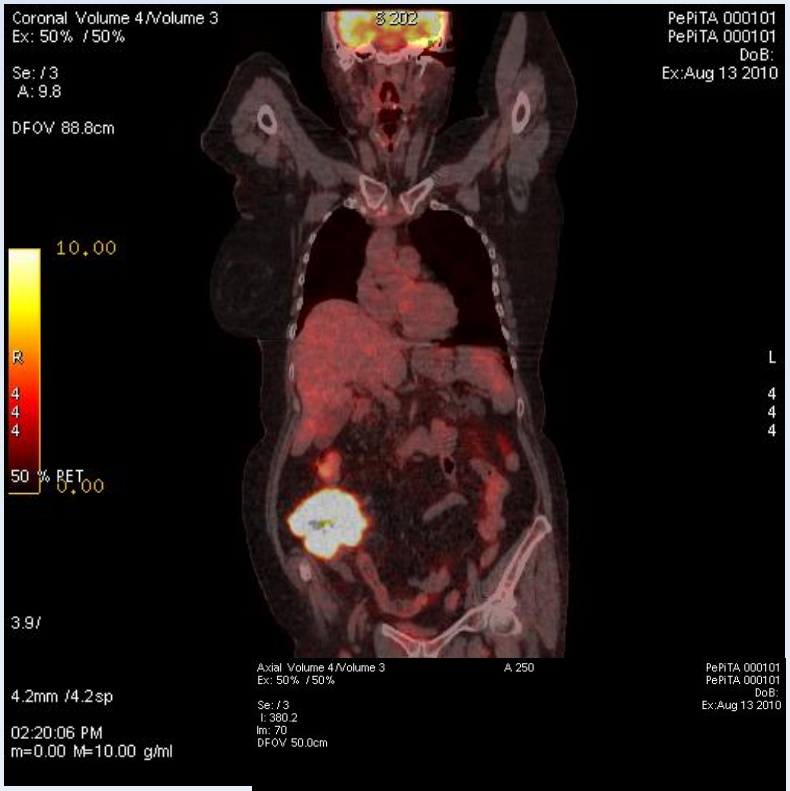


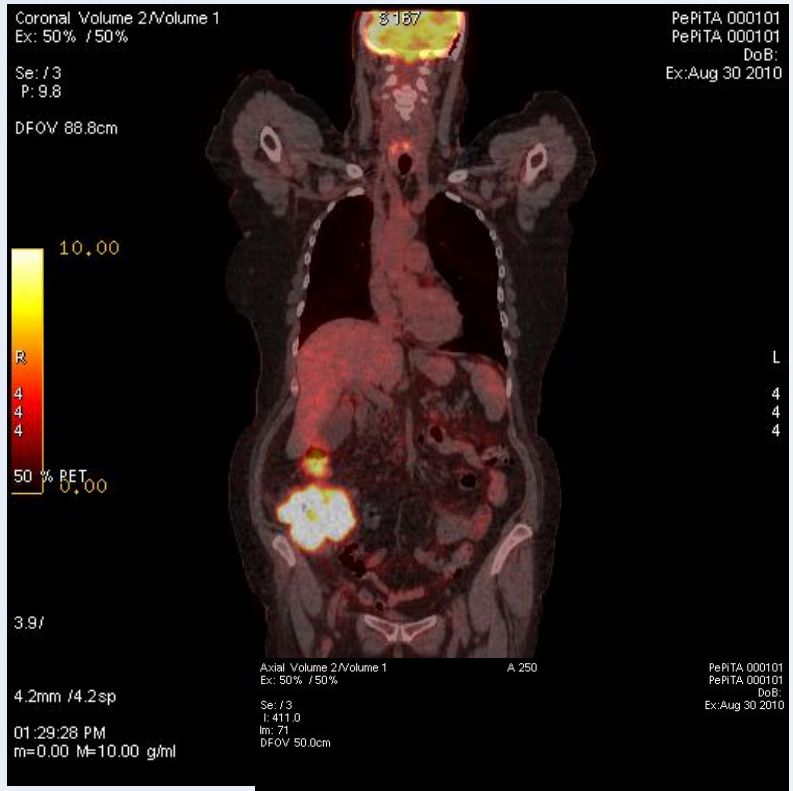
In Clinical Trials Setting …

PePiTA trial (NCT00994864)

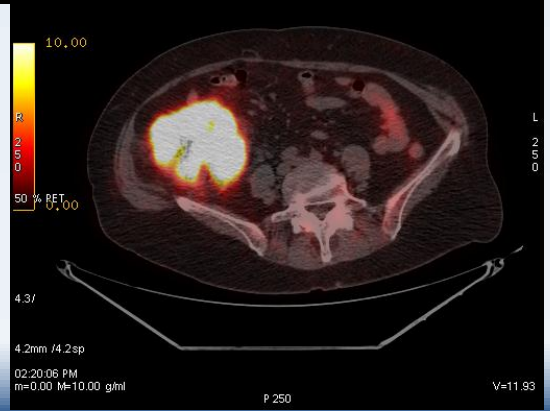


PePiTA trial : metabolic non response

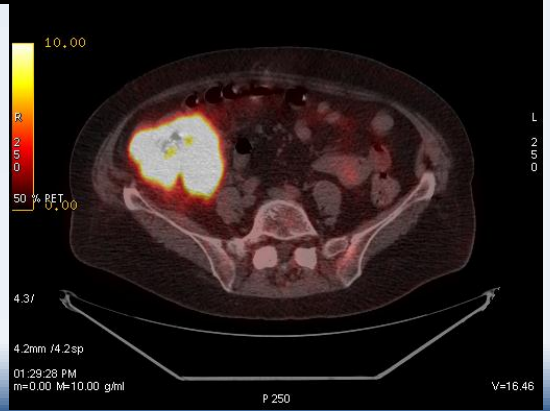




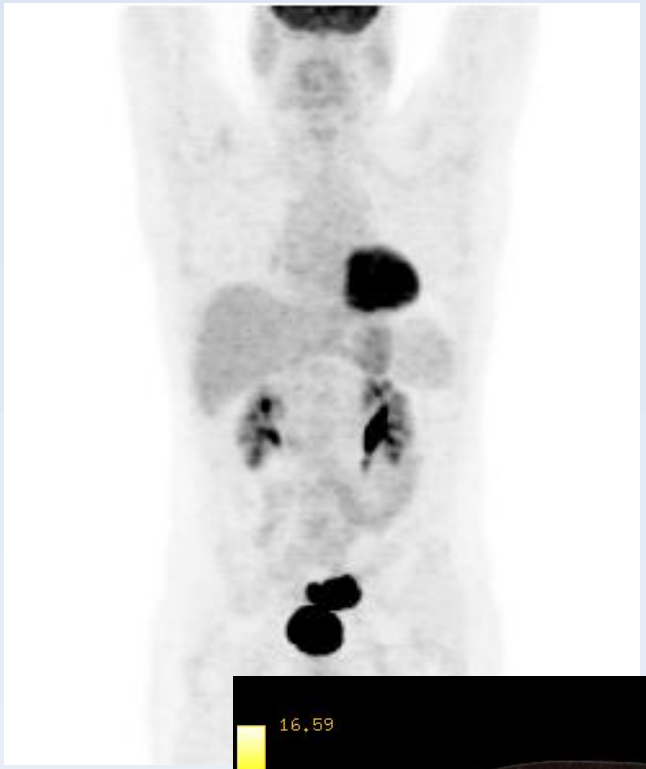
BASELINE PET

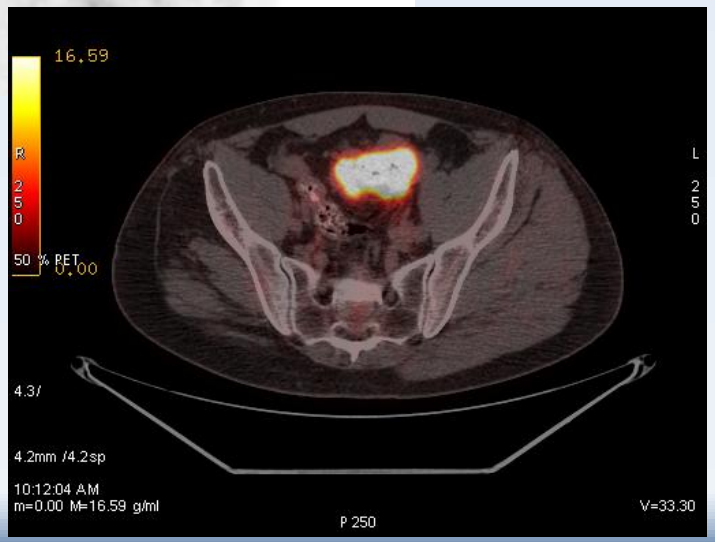


D14 PET

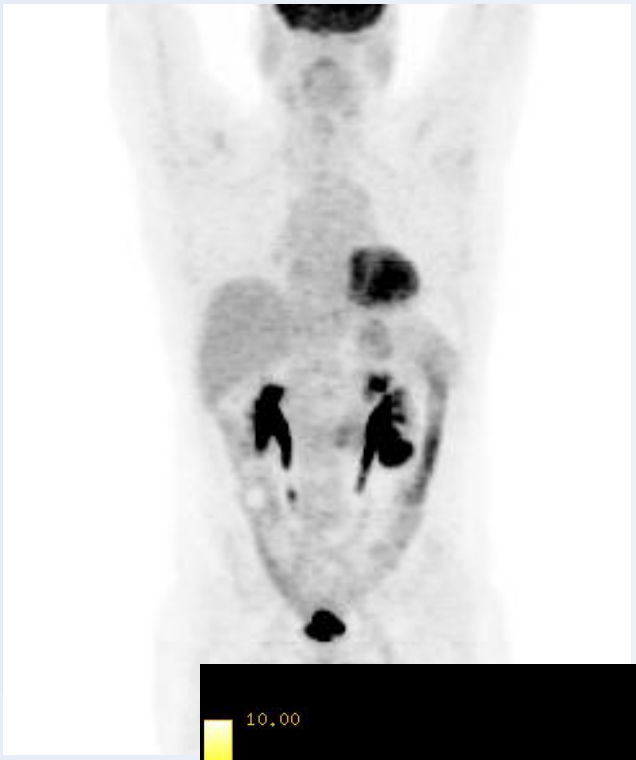


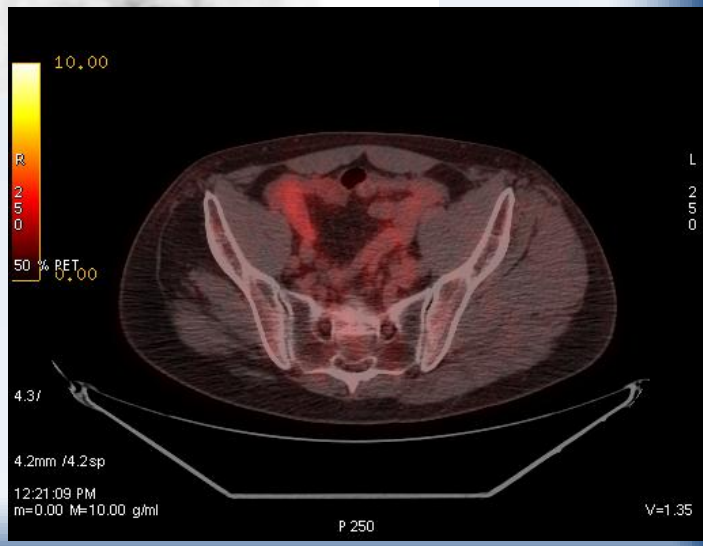
PePiTA trial : metabolic response





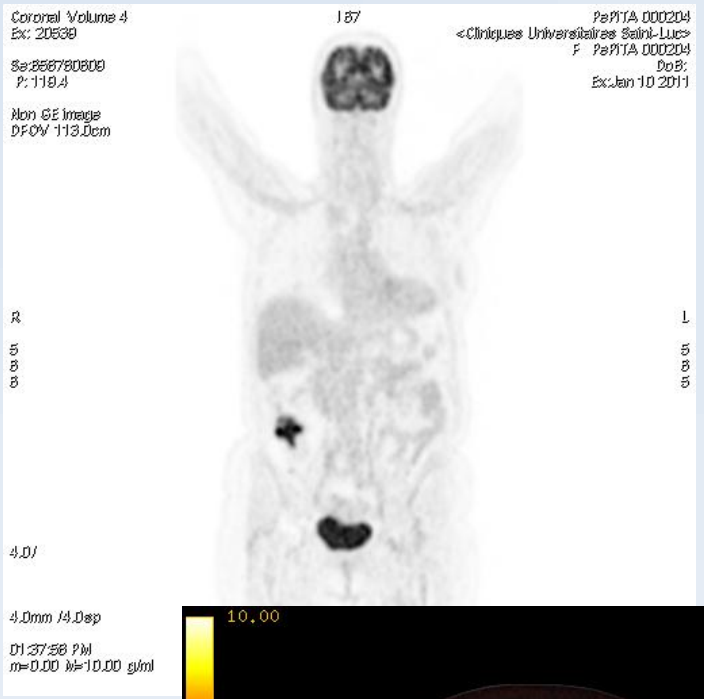
BASELINE PET

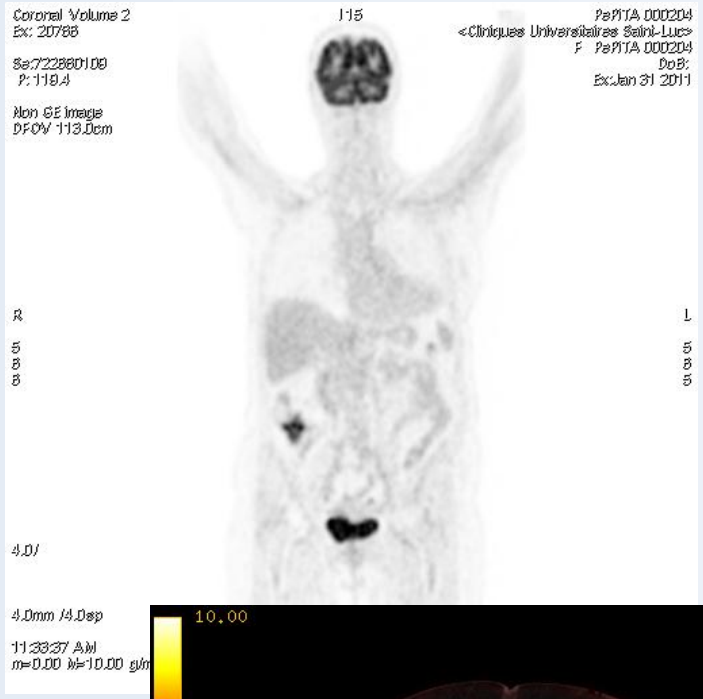




D14 PET

PePiTA trial : metabolic partial response





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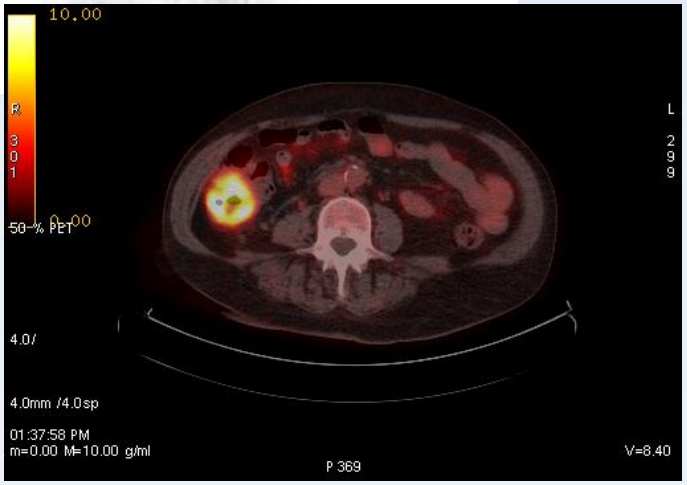
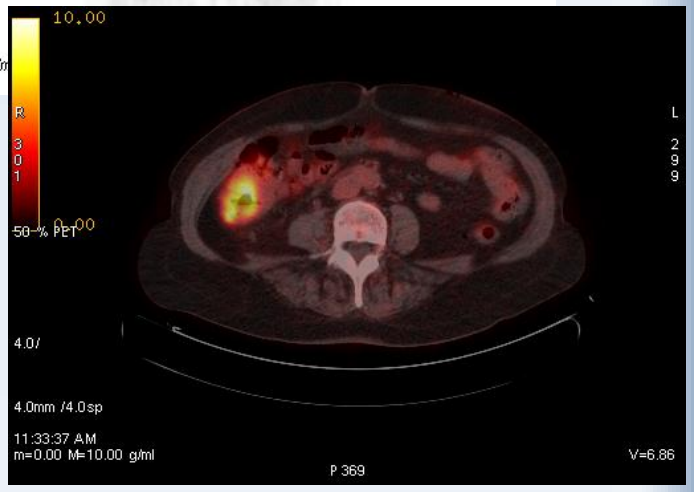
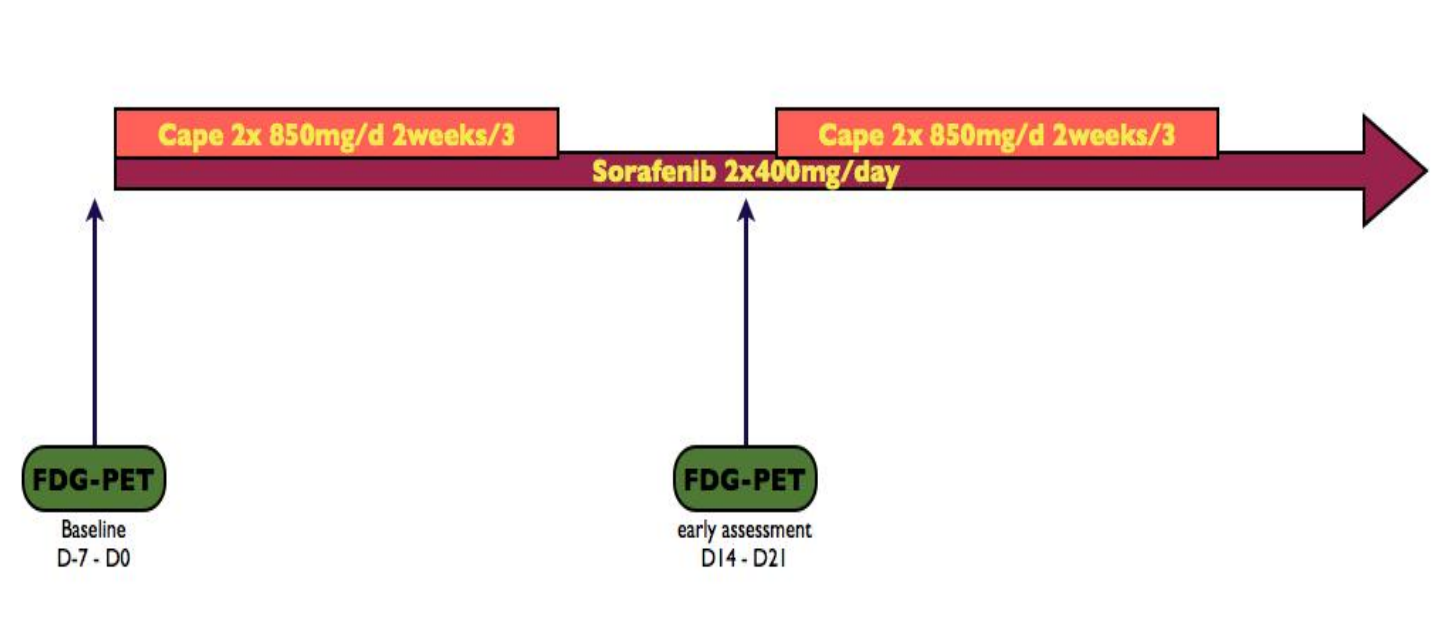


D14 PET



Delta SUV = - 31%

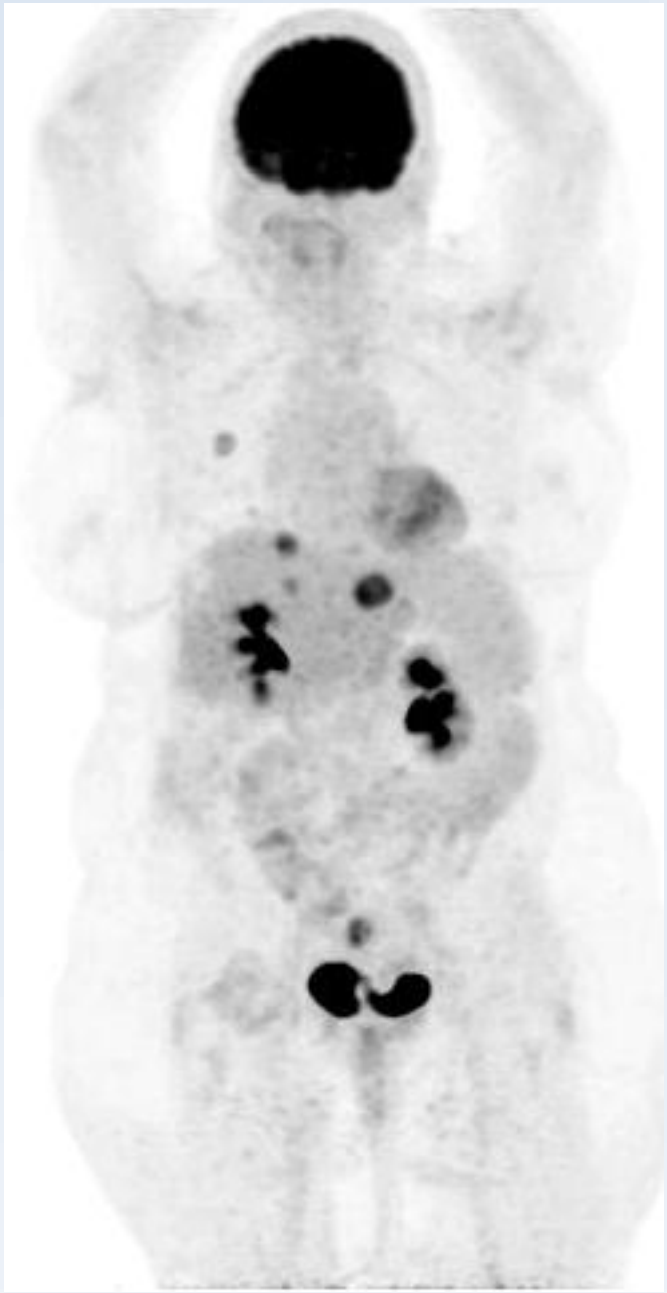
In Clinical Trials Setting …
The SoMore Study (NCT01290926)

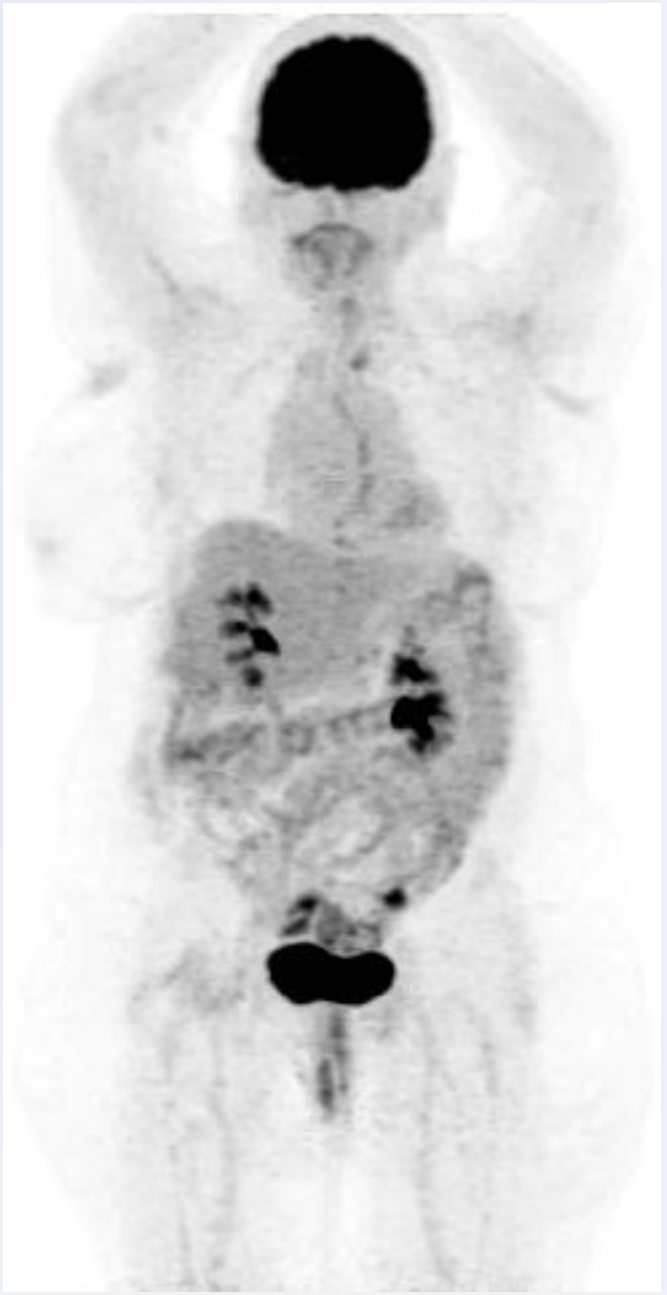


2 co-primary endpoints :

a) **OS** at a **fixed time point** (6 months)

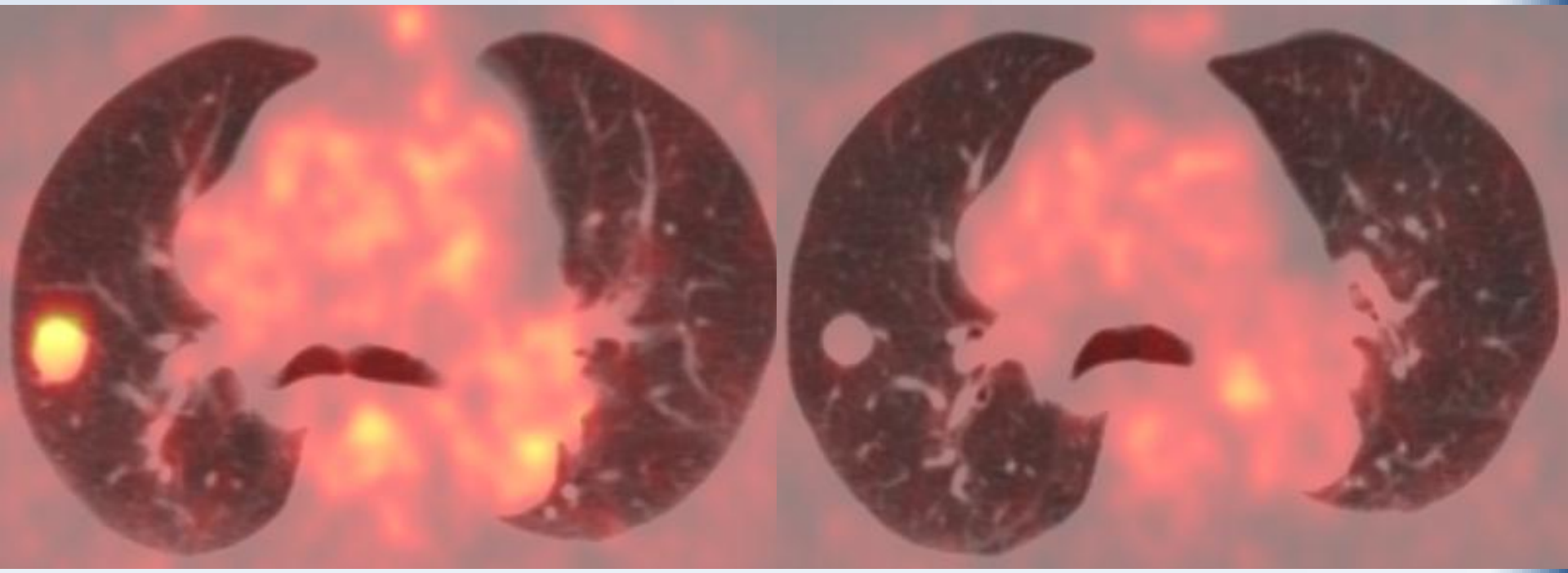
b) Compare **OS of metabolic responders versus non-responders**.

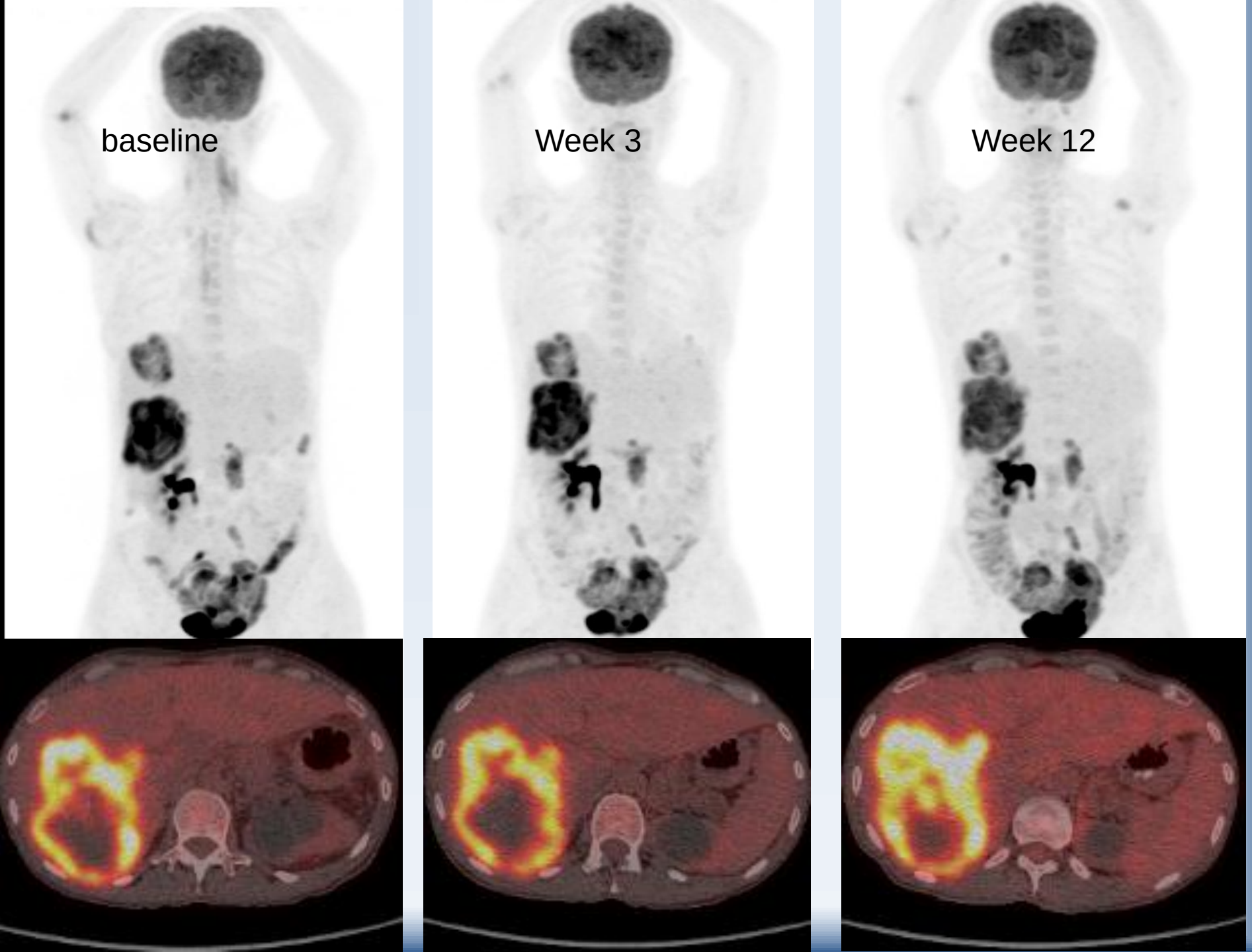




Baseline

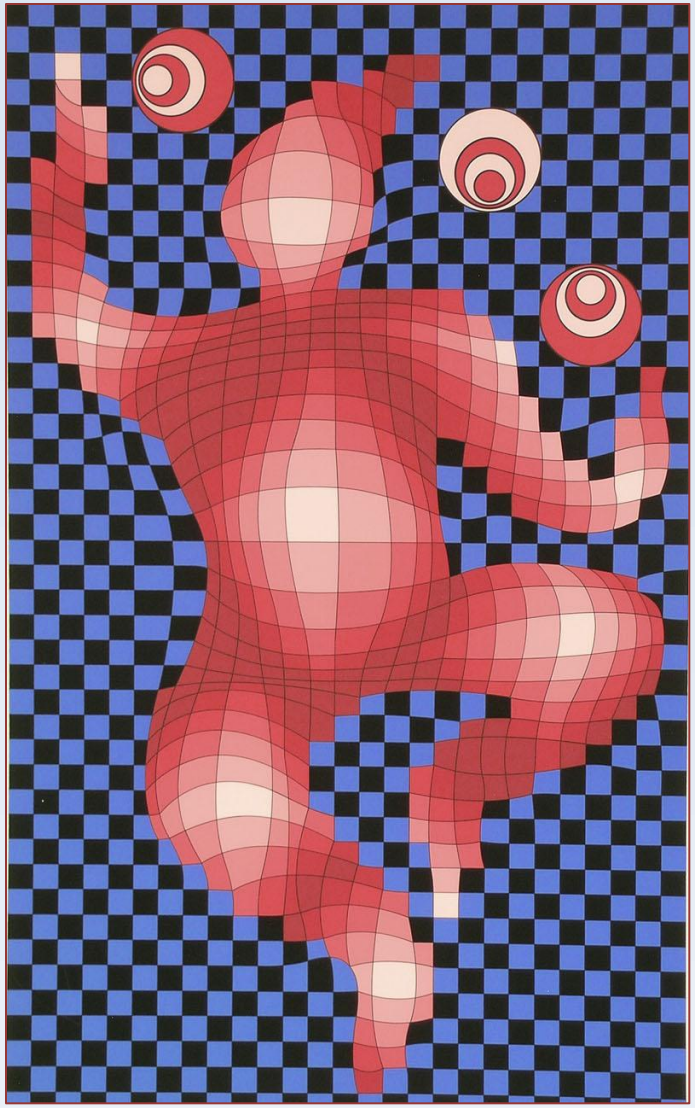
8 weeks




baseline
Week 3
Week 12

CONCLUSIONS

- **There is a need for more precise and faster assessment tools**
  - **in daily practice**
  - **in clinical trials**
- **Among candidates, FDG-PET is probably the most promising**
- **New tools should be used to**
  - better tailor treatment in daily practice
  - develop new trial concepts
  - develop new therapeutic algorythms
- **There is a lot more to learn …**



We thank the patients,

their family,

and all the collaborators.

What if everything is an illusion and nothing exists? In that case, I definitely overpaid for my carpet.

Woody Allen.

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