



Advances in Imaging

Molecular Imaging

Wim J.G. Oyen



Humanitas University and
Humanitas Clinical and Research Center
Milan, Italy

wim.oyen@hunimed.eu



Rijnstate Hospital
Arnhem, The Netherlands

woyen@rijnstate.nl

Disclosures

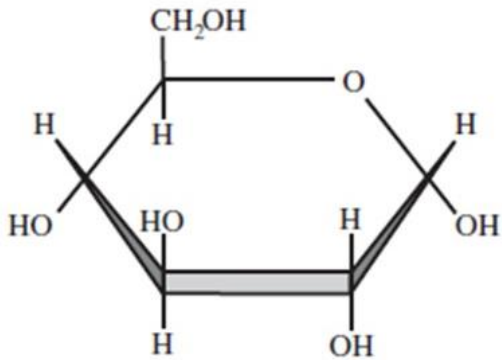
- **No disclosures**

What is Molecular Imaging ?

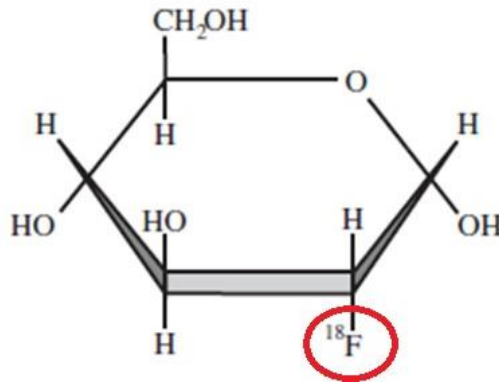
molecule

(linker)

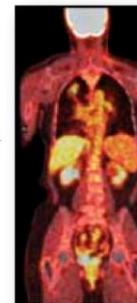
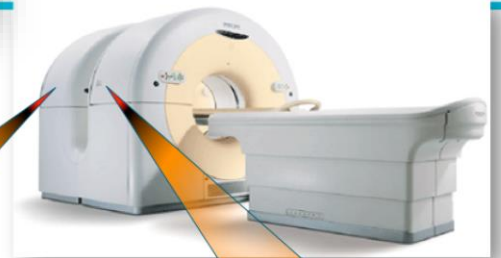
tag



glucose



FDG



Why Molecular Imaging ?

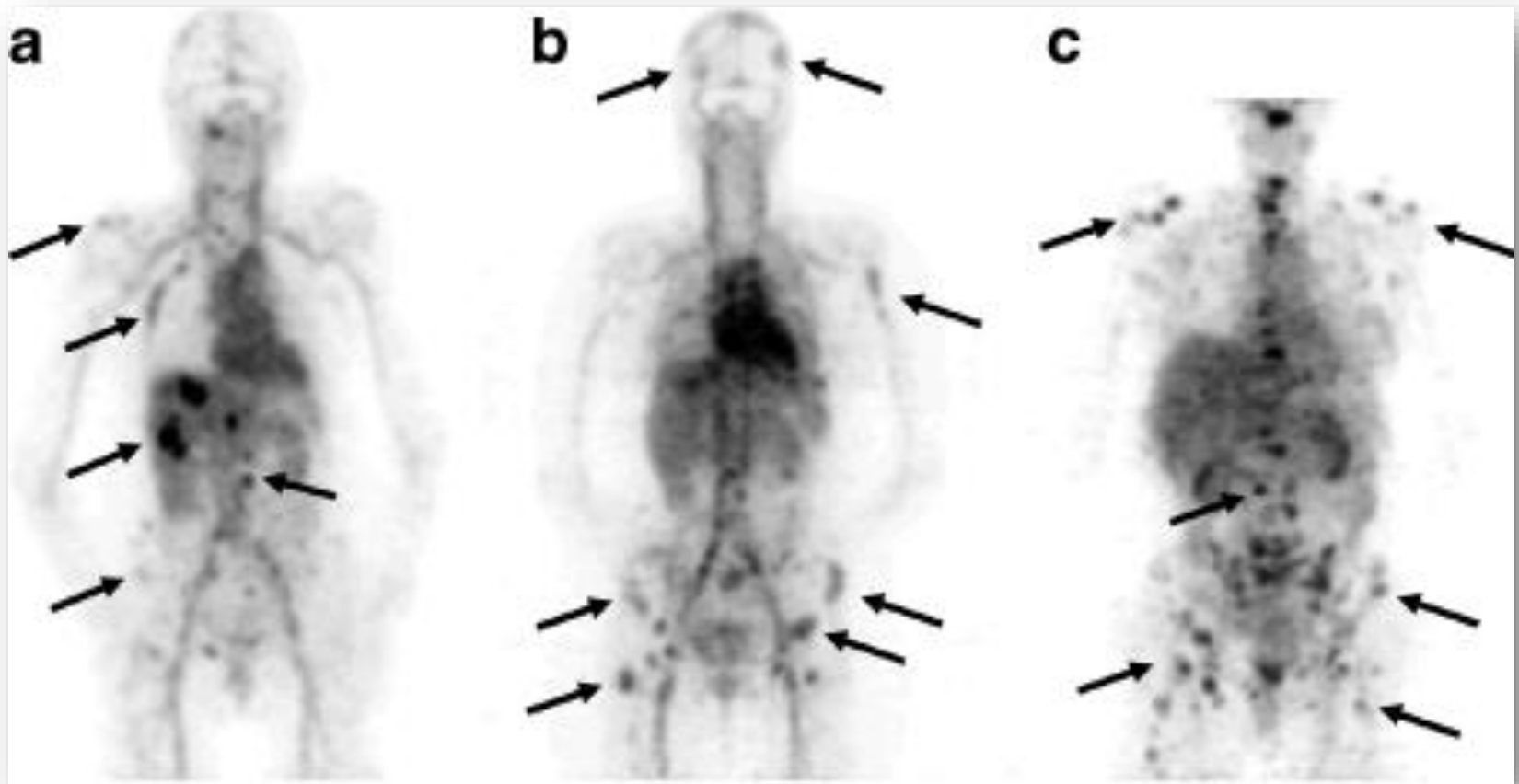
- Presence of the target : *is it there ?*
- Heterogeneity of expression : *is it on all lesions ?*
- Accessibility of the target : *does the drug reach it ?*
- Dose dependency : *how much drug is needed ?*
- Modulation of the target : *does expression change ?*
- Drug interactions : *impact of combination therapy ?*

Potential impact of molecular imaging

- Staging
- Tumor delineation
- **Characterization of tumors**
 - target expression
 - heterogeneity (intra & intertumoral)
 - prognostic biomarkers
- **Therapy response monitoring and prediction**
 - predictive biomarkers
 - early adaptation of ineffective treatment
 - interactions in multi-modality treatment
- **Follow-up / Relapse detection**

pivotal question: impact on patient management

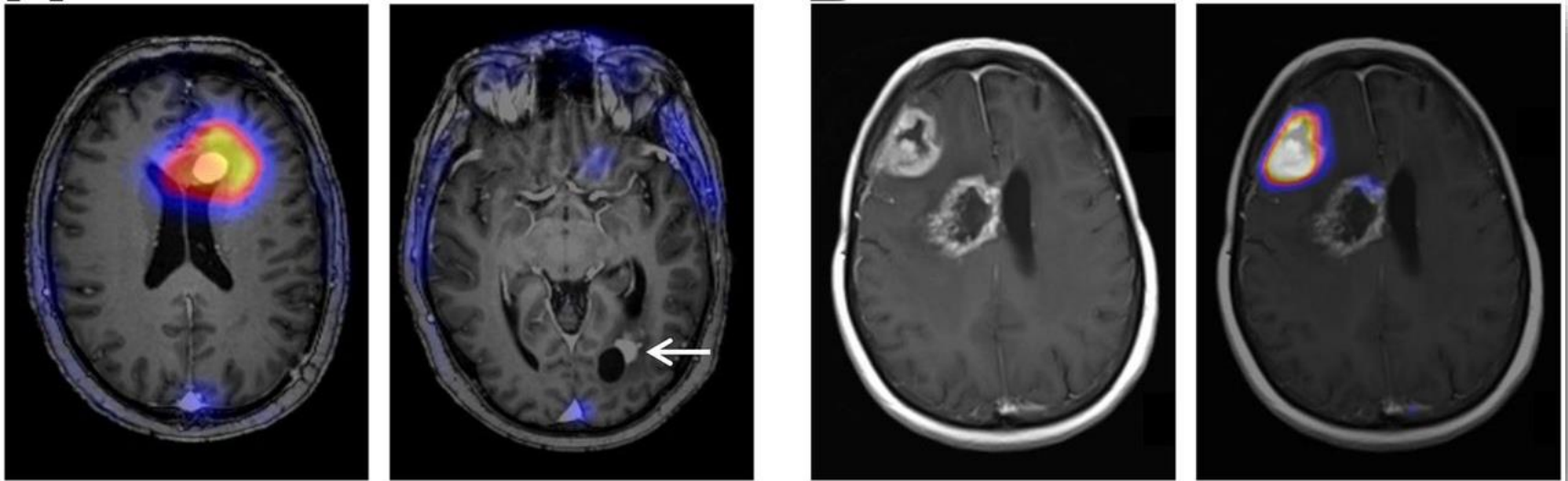
Target expression – Zr-89-trastuzumab



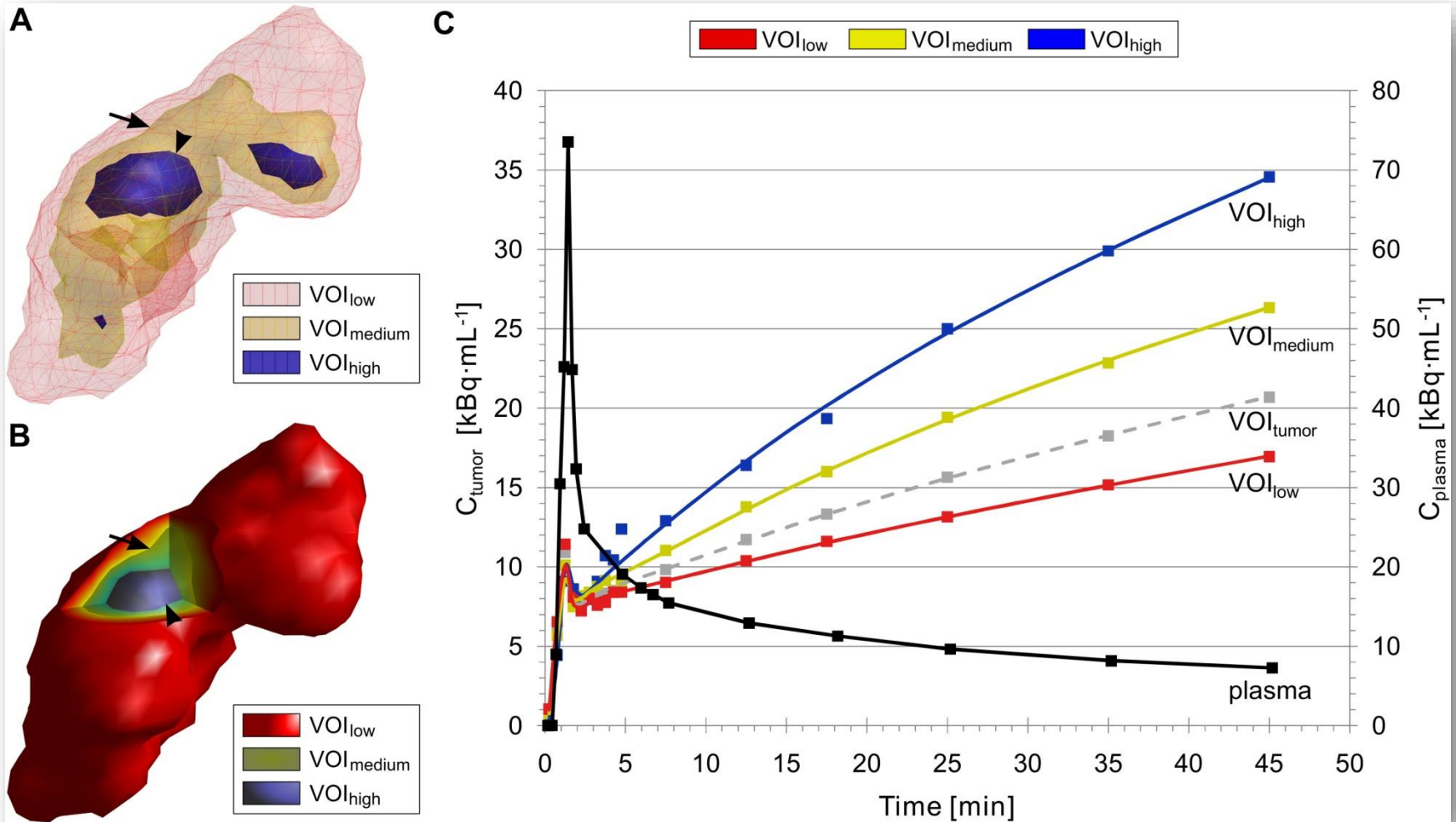
- 50 mg (drug-naïve) - 10 mg (on drug)
- Timing of imaging : 4-5 days p.i.

Is the target expressed and is it accessible ?

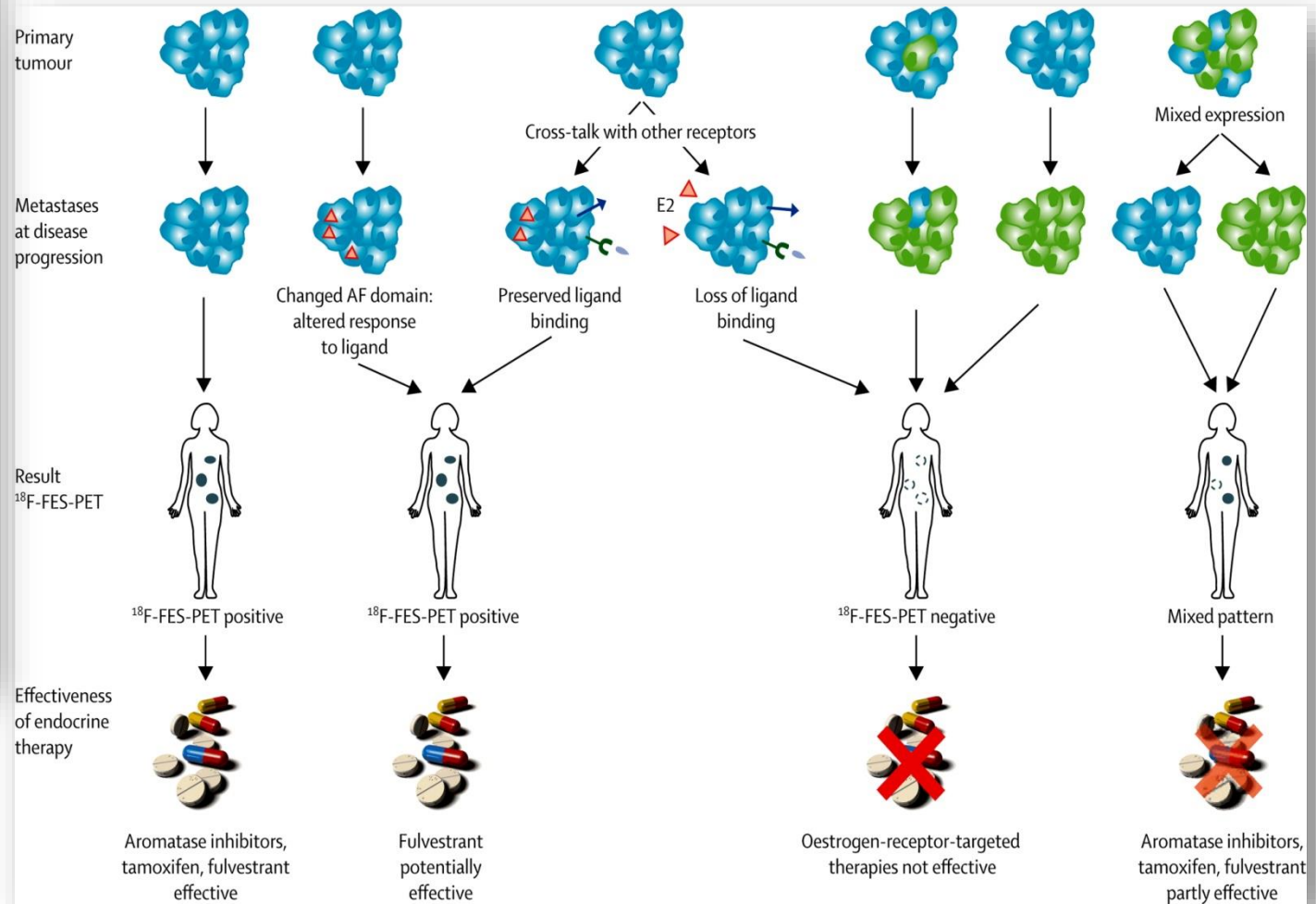
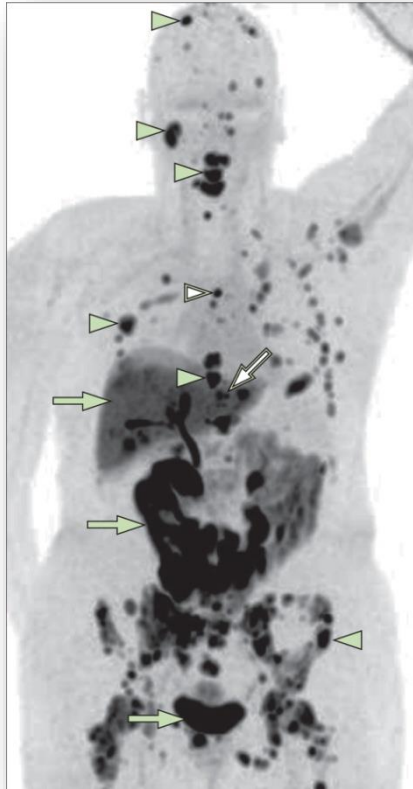
Zr-89-Fresolimumab (TGF- β) in recurrent glioma



Understanding tumor biology : *Heterogeneity*



Target expression and modulation - FES



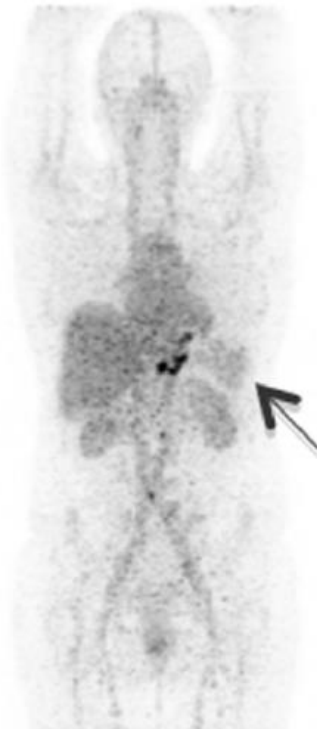
Rational dose finding

- Zr-89-Rituximab ImmunoPET -

No Preload



Preload



No Preload

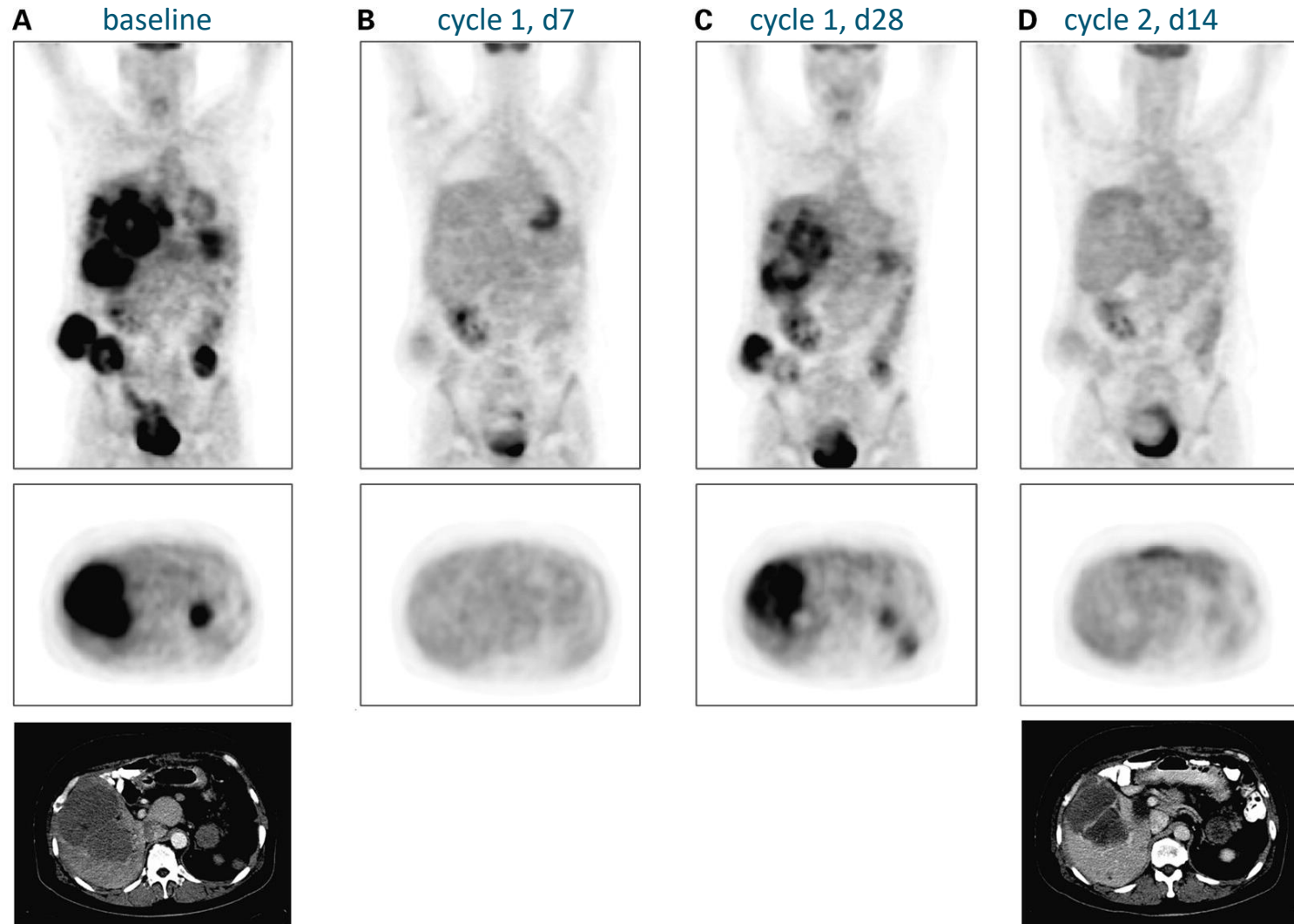


Preload



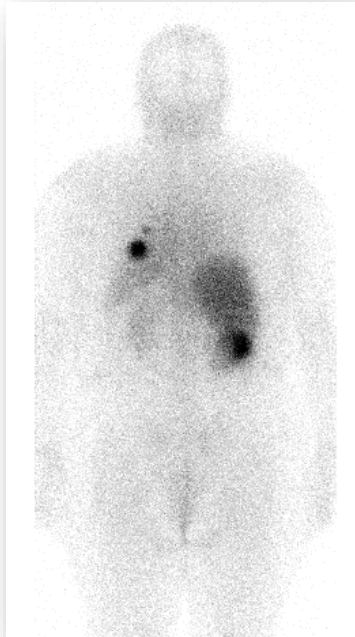
Assessing the Dosing Schedule

GIST during sunitinib (2 wks on/2 wks off)

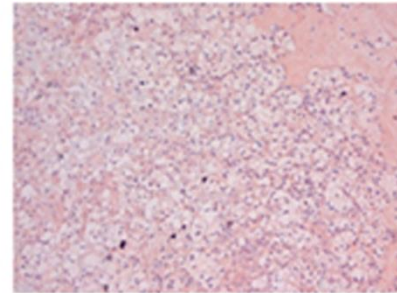
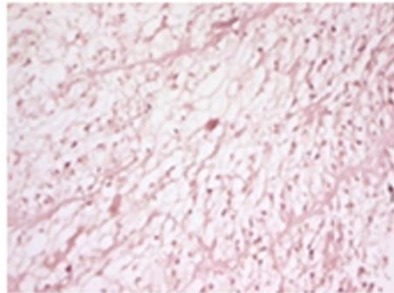


Depicting tumor biology, predicting response

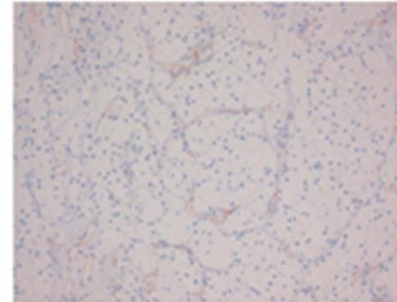
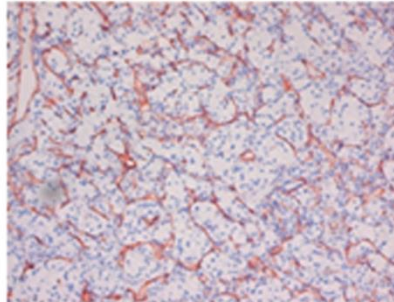
Before sorafenib



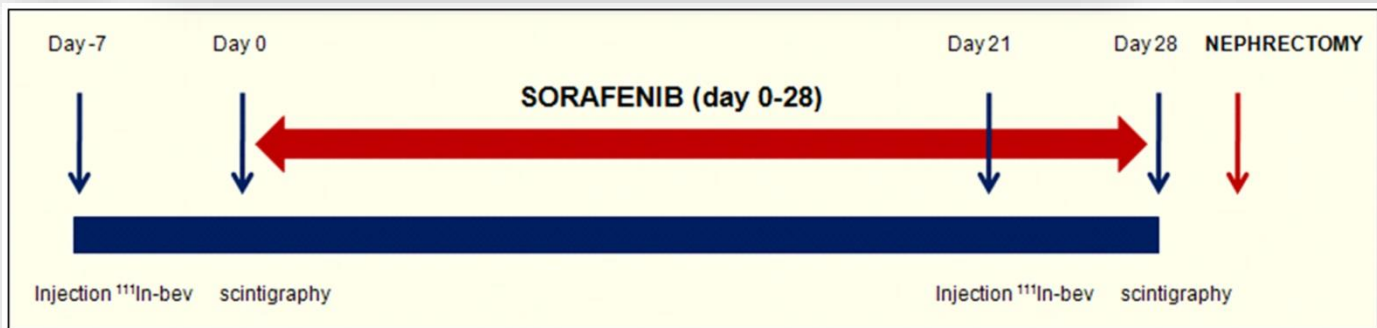
VEGF-A



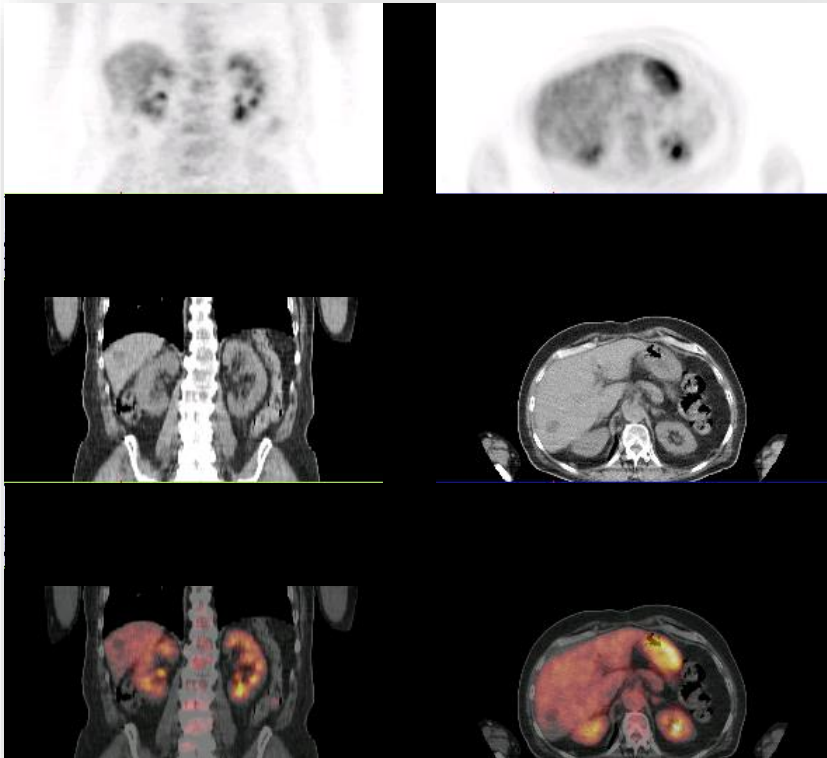
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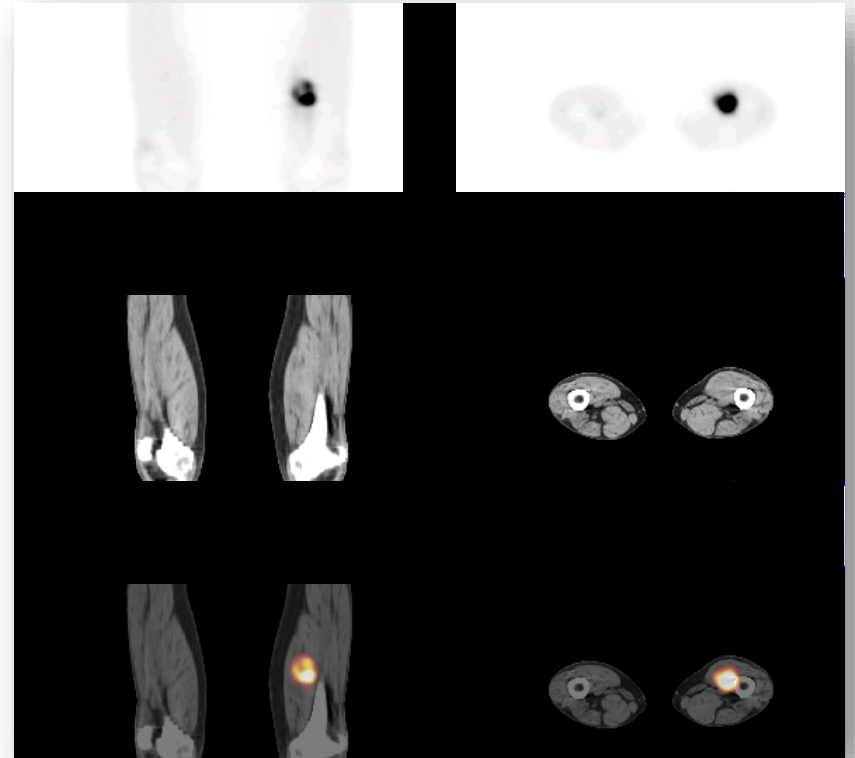
After 4 wks sorafenib



GIST: heterogeneity of metastases

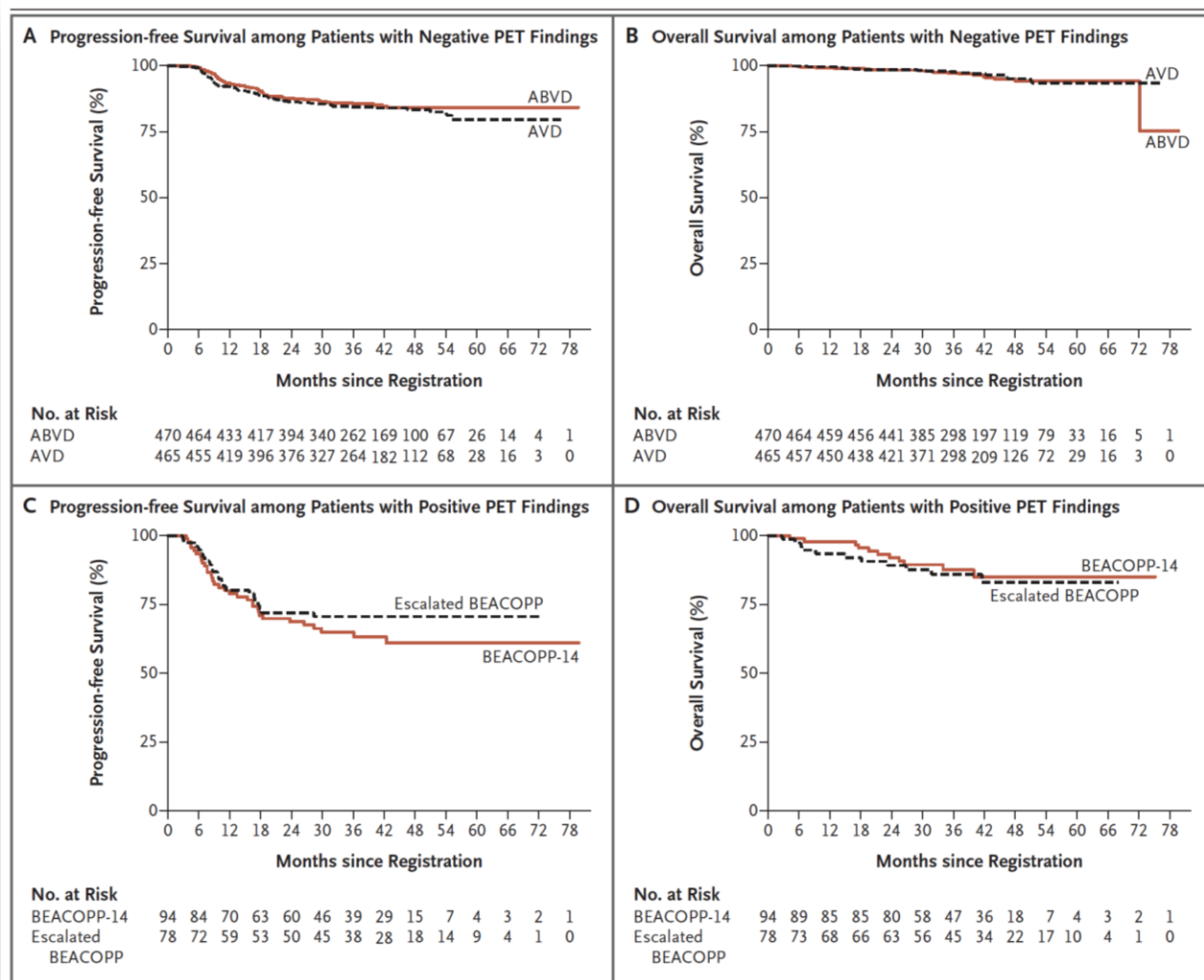


**Liver metastasis,
imatinib sensitive**



**Soft tissue metastasis,
imatinib resistant**

Early switch of regimen in advanced Hodgkin lymphoma : iPET2 guided treatment (RATHL)



The example of monitoring response in head and neck cancer

ORIGINAL ARTICLE

PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer

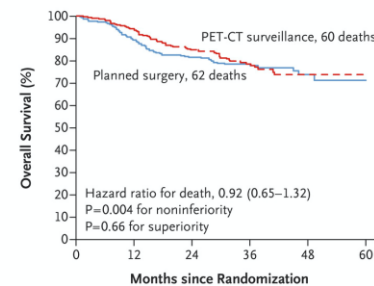
Hisham Mehanna, Ph.D., Wai-Lup Wong, F.R.C.R.,
Christopher C. McConkey, Ph.D., Joy K. Rahman, M.Sc.,
Max Robinson, Ph.D., Andrew G.J. Hartley, F.R.C.R., Christopher Nutting, Ph.D.,
Ned Powell, Ph.D., Hoda Al-Booz, F.R.C.R., Martin Robinson, F.R.C.R.,
Elizabeth Junor, F.R.C.R., Mohammed Rizwanullah, F.R.C.R.,
Sandra V. von Zeidler, Ph.D., Hulya Wiesmann, F.R.C.R., Claire Hulme, Ph.D.,
Alison F. Smith, M.Sc., Peter Hall, Ph.D., Janet Dunn, Ph.D.,
for the PET-NECK Trial Management Group*

CONCLUSIONS

Survival was similar among patients who underwent PET-CT-guided surveillance and those who underwent planned neck dissection, but surveillance resulted in considerably fewer operations and it was more cost-effective. (Funded by the National Institute for Health Research Health Technology Assessment Programme and Cancer Research UK; PET-NECK Current Controlled Trials number, ISRCTN13735240.)

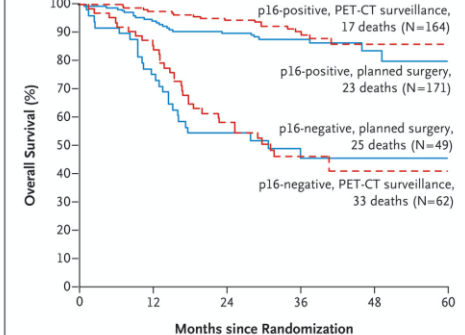
N ENGL J MED 374:15 NEJM.ORG APRIL 14, 2016

A PET-CT Surveillance vs. Planned Neck Dissection, All Patients

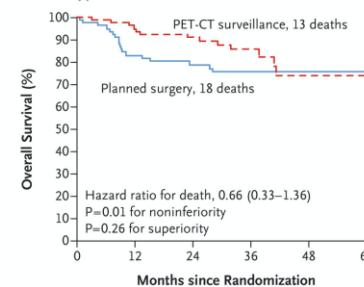


No. at Risk	0	12	24	36	48	60
Planned surgery	282	243	204	118	32	8
PET-CT surveillance	282	259	224	110	33	6

B PET-CT Surveillance vs. Planned Neck Dissection, According to Status of p16 Expression

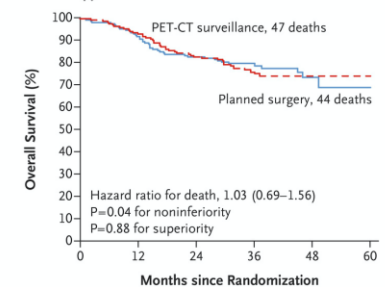


C PET-CT Surveillance vs. Planned Neck Dissection before Chemoradiotherapy



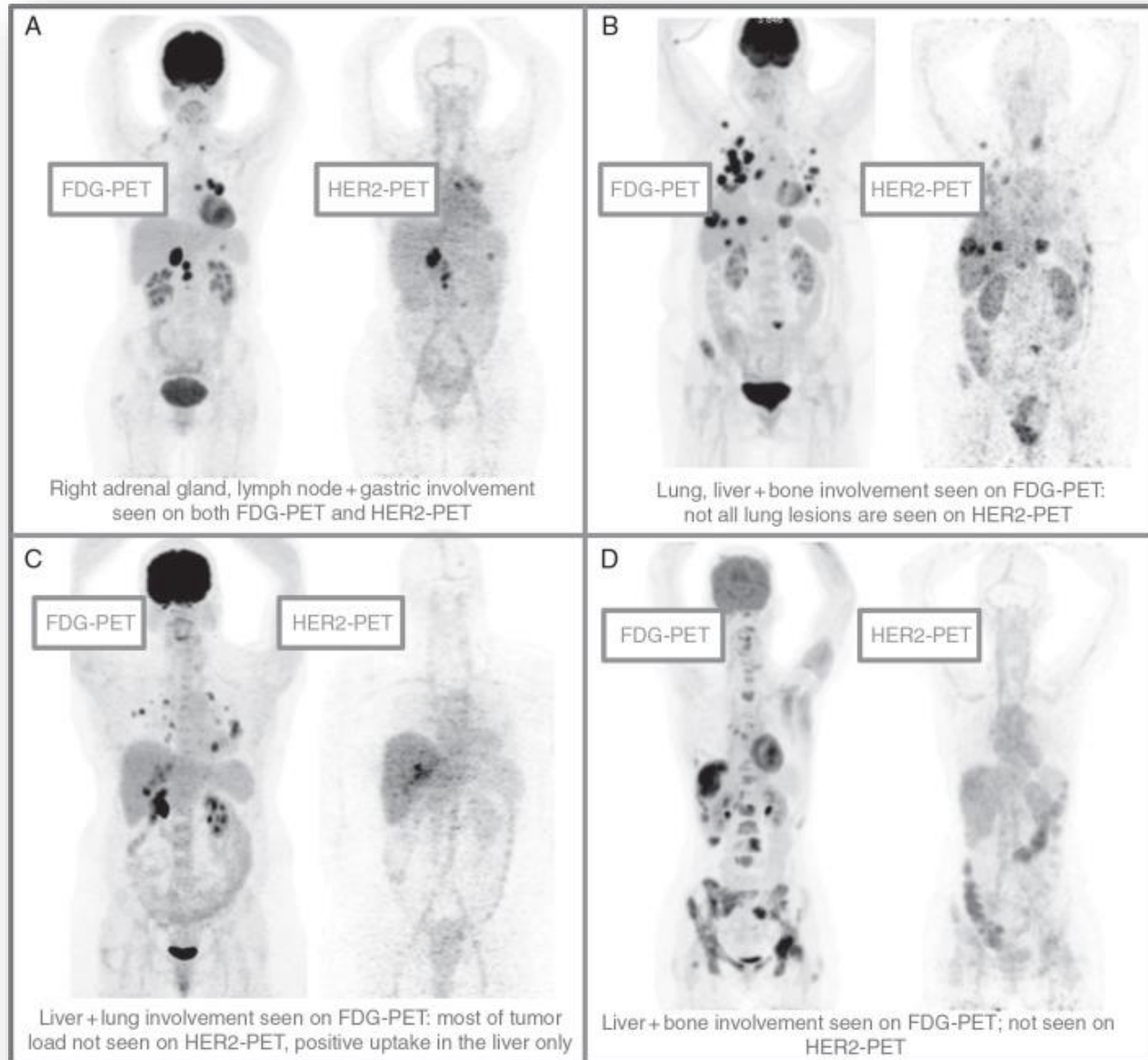
No. at Risk	0	12	24	36	48	60
Planned surgery	77	62	51	31	12	6
PET-CT surveillance	76	70	65	32	10	4

D PET-CT Surveillance vs. Planned Neck Dissection after Chemoradiotherapy



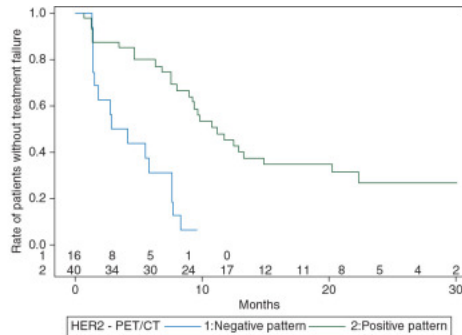
No. at Risk	0	12	24	36	48	60
Planned surgery	205	181	153	87	20	2
PET-CT surveillance	206	189	159	78	23	2

T-DM1 treatment in HER2[+] breast cancer - ZEPHIR trial

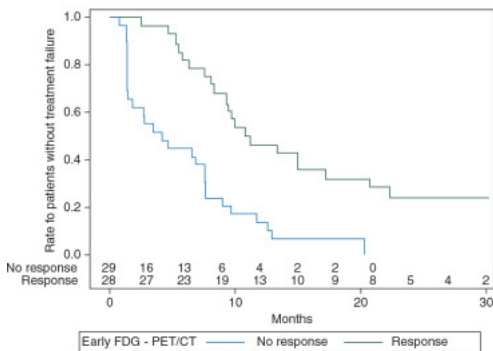


T-DM1 treatment in HER2[+] breast cancer - Zephir trial

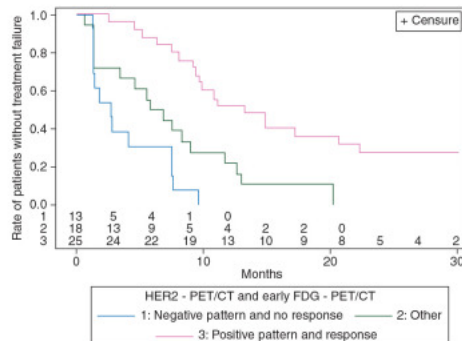
Median Time to Treatment Failure :



- * HER2[+] 11.2 mo (95% CI 8–15 mo);
- * HER2[-] 3.5 mo (95% CI 1.4–7.6 mo).
- HR 4.5 (95% CI 2.1–9.4, $P < 0.0001$)



- * early FDG–PET/CT response 13.3 mo (95% CI 9.3 mo–n.r.)
- * early FDG–PET/CT nonresponse 4.2 mo (95% CI 1.4–7.6 mo)
- HR 3.8 (95% CI 2–7.4, $P < 0.0001$)



- * HER2[+]/early FDG–PET/CT response 15 mo (95% CI 9.7 mo–n.r.)
- * HER2[-]/early FDG–PET/CT nonresponse 2.8 mo (95% CI 1.4–7.6 mo)
- HR 8.3 ($P < 0.0001$)
- * Discordant imaging results 6.3 mo (95% CI 1.4–9.0 mo)
- HR 3.7 ($P < 0.0001$)

What next ?

- Adhere to rigorous methodology, standardization and quality control
- Early inclusion in drug development to explore the potential
- Reponse vs. non-response assessment
- Prognosis and prediction → tailored and adaptive multimodality treatment
- Clinical trial objectives : from descriptive statistics to clinical impact
- Paying attention to generating the clinical evidence



CDDF

Cancer Drug Development Forum



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2021