PRESENTATION 93MO

ESMO BREAST CANCER

Onsite and Online Congress

OPTIMAL ^{18}F-FDG-PET CUTOFF VALUE FOR pCR PREDICTION IN HER2-POSITIVE EARLY-STAGE BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT TRASTUZUMAB AND PERTUZUMAB IN THE PHERGain TRIAL

G. Gebhart, M. Keyaert, T. Guiot, P. Flamen, M.R. Borrego, A. Stradella, B. Bermejo, S. Escriva-de-Romani, L. Calvo Martínez, N. Ribelles, N. Martinez, C. Albacar, M. Colleoni, M. Atienza de Frutos, M. Sampayo, J. Cortés, J.M. Pérez-Garcia, A. Llombart-Cussac

Geraldine Gebhart, MD
Institute Jules Bordet, Brussels, Belgium
geraldine.gebhart@bordet.be

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

MEDSIR MEDICA SCIENTIA INNOVATION RESEARCH

INSTITUT JULES BORDET

DECLARATION OF INTERESTS

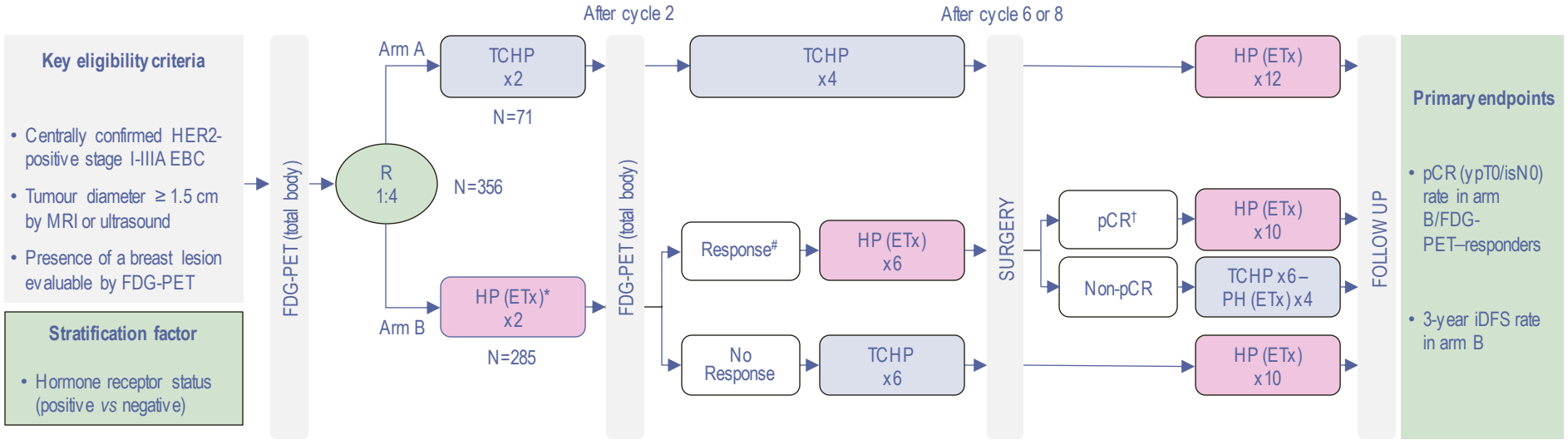
Geraldine Gebhart, MD

Advisory board, Research funding (no personal funds accepted, institutional only):

Roche

PHERGain STUDY DESIGN

PHERGain is assessing the potential of metabolic imaging to identify candidates for chemotherapy de-escalation in HER2-positive, stage I–IIIA, invasive, operable breast cancer with at least one breast lesion evaluable by FDG-PET.



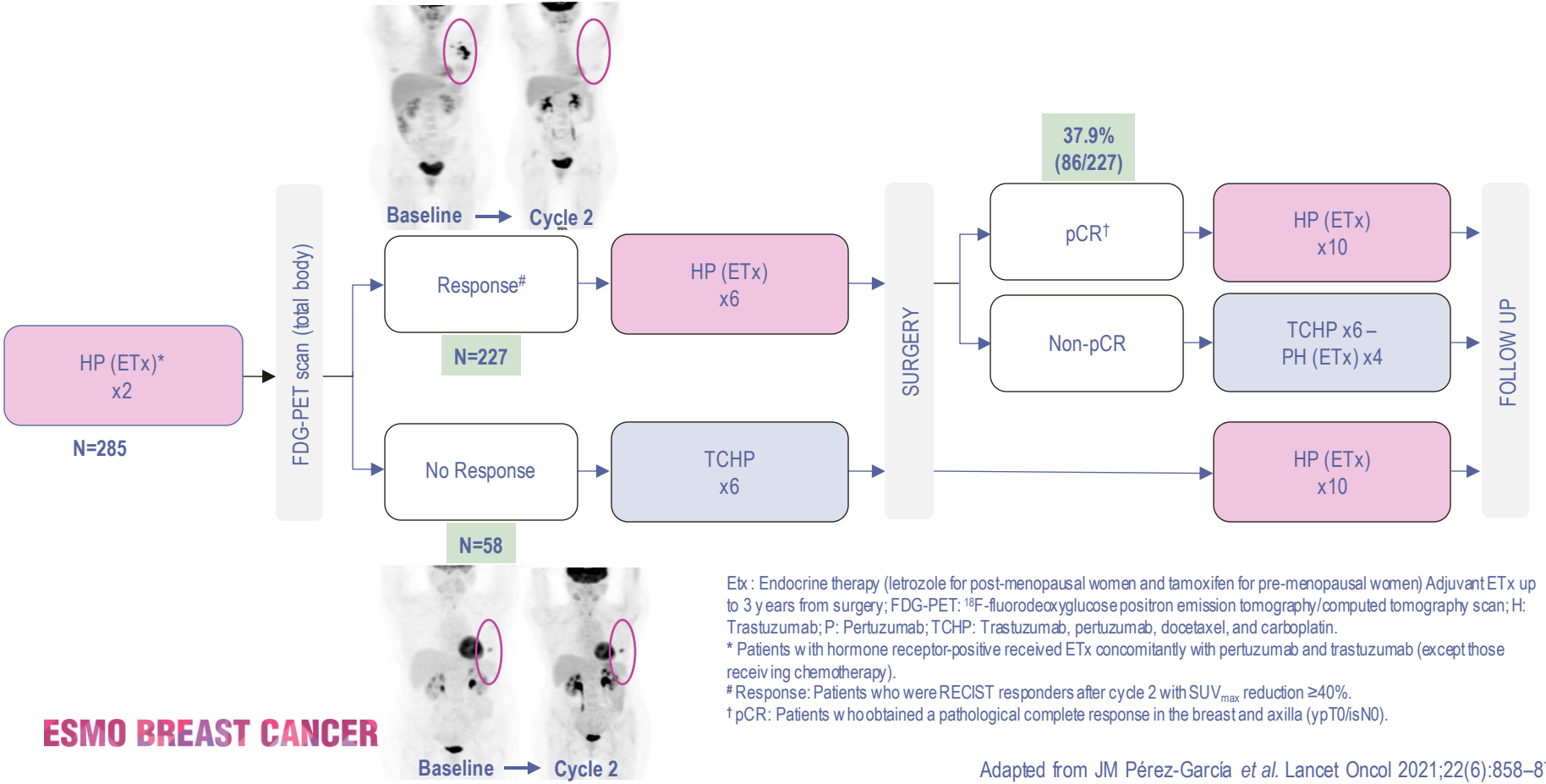
EBC: Early breast cancer; Etx: Endocrine therapy (letrozole for post-menopausal women and tamoxifen for pre-menopausal women) Adjuvant ETx up to 3 years from surgery; FDG-PET: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan; H: Trastuzumab; HER2: Human epidermal growth factor receptor 2; iDFS: Invasive disease-free survival; P: Pertuzumab; R: Randomization; TCHP: Trastuzumab, pertuzumab, docetaxel, and carboplatin.

* Patients with hormone receptor-positive received ETx concomitantly with pertuzumab and trastuzumab (except those receiving chemotherapy).

Response: Patients who were RECIST responders after cycle 2 with SUV_{max} reduction ≥40%.

† pCR: Patients who obtained a pathological complete response in the breast and axilla (ypT0/isN0).

pCR RATE IN ARM B/FDG-PET–RESPONDERS WITH SUV$_{max}$ REDUCTION ≥40%



Etx : Endocrine therapy (letrozole for post-menopausal women and tamoxifen for pre-menopausal women) Adjuvant ETx up to 3 years from surgery; FDG-PET: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan; H: Trastuzumab; P: Pertuzumab; TCHP: Trastuzumab, pertuzumab, docetaxel, and carboplatin.
* Patients with hormone receptor-positive received ETx concomitantly with pertuzumab and trastuzumab (except those receiving chemotherapy).
# Response: Patients who were RECIST responders after cycle 2 with SUV$_{max}$ reduction ≥40%.
† pCR: Patients who obtained a pathological complete response in the breast and axilla (ypT0/isN0).

Adapted from JM Pérez-García *et al.* Lancet Oncol 2021;22(6):858–871

STUDY AIM

As a secondary preplanned analysis of the PHERGain trial, we aimed to select the best cutoff value of SUV_{max} reduction (ΔSUV_{max}) at 6 weeks of trastuzumab and pertuzumab (plus endocrine therapy if hormone receptor-positive) for pCR prediction.

STATISTICAL METHODS

- We randomly splitted the PHERGAIN dataset in:
  - a) **Training dataset** (80%) for selection of the best cutoff of the ΔSUV_{max} based on sensitivity and positive predictive values (PPV) using cross-validation method;
  - b) **Test dataset** (20%) for validation of the optimal cutoff selected in the training dataset.
- We calculated a 95% confidence interval (CI) for the ΔSUV_{max} optimal cutoff, based on the correlation between the ΔSUV_{max} values of the two FDG-PET evaluators.
- The upper boundary for the interval was defined as the final cutoff. It maximizes the probability of achieving a pCR in patients who will avoid chemotherapy ($\Delta SUV_{max} \geq$ cutoff).
- We evaluated Area Under the Receiver Operating Characteristic Curve (AUC) and computed 95% CI using the De Long method.

DEMOGRAPHIC AND BASELINE CLINICAL CHARACTERISTICS IN ARM B/FDG-PET–RESPONDERS

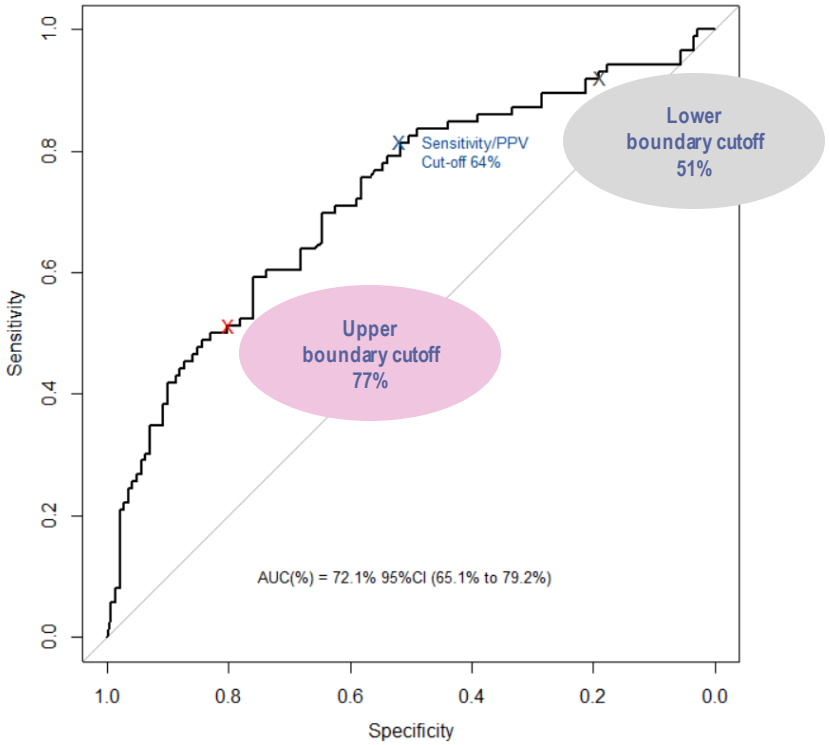
MEDSIR
MEDICA SCIENTIA INNOVATION RESEARCH

Characteristic	Arm B/FDG-PET–Responders (n=227)	Pts who achieve pCR (n=86)	Pts who did not achieve pCR (n=141)	*P* value
Age, median (IQR), years	51 (45.0–59.0)	52 (45.2–60.8)	50 (45.0–58.0)	0.372
Postmenopausal				
No	117 (51.5)	41 (47.7)	76 (53.9)	0.363
Yes	110 (48.5)	45 (52.3)	65 (46.1)	
Stage				
I	21 (9.3)	10 (11.6)	11 (7.8)	0.34
II	173 (76.2)	64 (74.4)	109 (77.3)	
IIIA	33 (14.5)	12 (14)	21 (14.9)	
Nodal status				
Negative	117 (51.5)	49 (57)	68 (48.2)	0.201
Positive	110 (48.5)	37 (43)	73 (51.8)	
Hormone receptor status				
ER-negative and PR-negative	70 (30.8)	31 (36)	39 (27.7)	0.185
ER-positive or PR-positive, or both	157 (69.2)	55 (64)	102 (72.3)	
HER2 IHC score and FISH analysis				
2+ and FISH-positive	43 (18.9)	11 (12.8)	32 (22.7)	0.068
3+	184 (81.1)	75 (87.2)	109 (77.3)	
SUV_{max} at baseline, median (IQR)	10.4 (6.2–15.5)	8.8 (5.6–15.5)	10.8 (6.8–15.4)	0.248
SUV_{max} at cycle 2, median (IQR)	2.2 (1.3–3.6)	1.6 (0.7–2.6)	2.7 (1.7–4.7)	**<0.001**
ΔSUV_{max}, median (IQR) ***	-69.6 (-57.5—79.9)	-77.8 (-67—85.4)	-63.3 (-54.8—74.8)	**<0.001**

ESMO BREAST CANCER

Data are n (%), unless otherwise specified. ER: Estrogen receptor; FISH: Fluorescence *in situ* hybridization; IHC: Immunohistochemistry; PR: Progesterone receptor; Pts: Patients; SUV_{max}: The maximum Standardized Uptake Value.

SENSITIVITY AND SPECIFICITY TO PREDICT pCR FOR THE DIFFERENT ΔSUV_{max} CUTOFF VALUES IN ARM B/FDG-PET–RESPONDERS



ASSOCIATION BETWEEN ΔSUV_{max} CUTOFF VALUES AND pCR

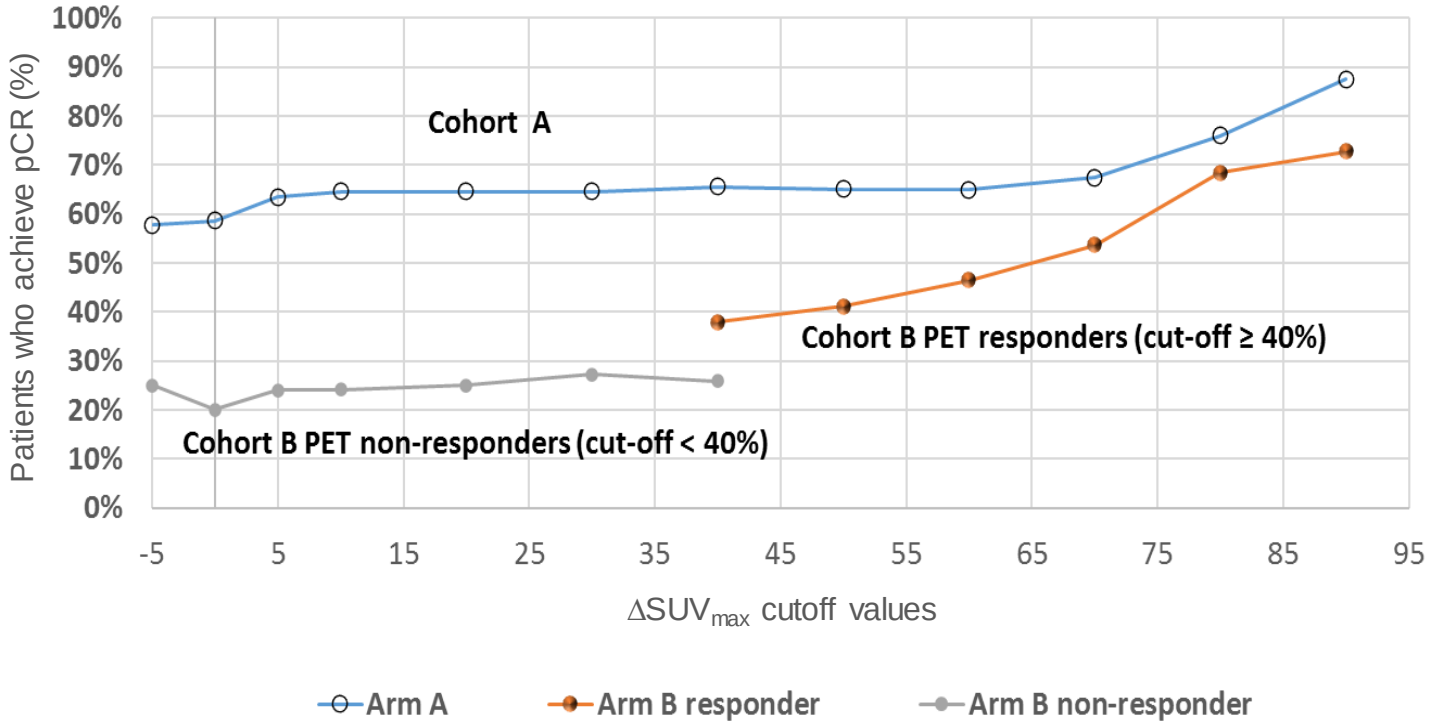
ΔSUV_{max} cutoff value	Pts meeting the ΔSUV_{max} cutoff value with no CTx, n (%)	Pts who receive neoadjuvant CTx, n	Pts who achieve pCR after receiving no CTx, %	Pts who achieve pCR after receiving PH (+/- ETx), n	Pts who receive adjuvant CTx, n	Pts expected to receive CTx among 285 pts, n (%)
≥40%	227 (85.0)	58	37.9	86	141	199 (70.0)
≥51%	192 (67.4)	93	41.0	79	113	206 (72.0)
≥64%	140 (49.1)	145	50.0	70	70	215 (75.4)
≥77%	74 (26.0)	211	59.5	44	30	241 (84.5)
↓	↓	↓	↓		↓	
The higher the ΔSUV_{max} cutoff value…	…the fewer pts meet the selected cutoff value…	…the more pts receive neoadjuvant CTx…	…the more pts achieve pCR…		…the fewer pts need adjuvant CTx	

- **ΔSUV_{max} ≥40% remains the cutoff value that allows to spare most pts from CTx.**

ESMO BREAST CANCER

CTx: Chemotherapy; ETx: Endocrine therapy; H: Trastuzumab; P: Pertuzumab; pCR: Pathological complete response; Pts: Patients; SUV_{max}: The maximum Standardized Uptake Value

ASSOCIATION BETWEEN ΔSUV_{max} CUTOFF VALUES AND pCR IN COHORTS A AND B



CONCLUSIONS

- The ΔSUV_{max} ≥77% after two cycles of trastuzumab and pertuzumab achieves a pCR rate in the range of control arm with chemotherapy plus trastuzumab and pertuzumab (59.5% vs. 57.7%, respectively), selecting a subgroup of patients with HER2 addicted tumors.
- However, the original ΔSUV_{max} ≥40% maximizes the number of patients who could avoid chemotherapy.
- Interestingly, the TBCRC026 phase 2 trial also demonstrated that early ΔSUV_{max} ≥40% predicts pCR of stage II or III, estrogen receptor-negative, HER2-positive breast cancer after four cycles of neoadjuvant trastuzumab and pertuzumab.[1]
- The definitive value of pCR in the absence of chemotherapy and FDG-PET–based pathological response–adapted strategy in PHERGain should be confirmed by the 3-year invasive disease-free survival.

[1] RM Connolly, *et al.* J Clin Oncol 2021;39(20):2247–2256

ACKNOWLEDGEMENTS

- Patients and their families.
- Investigators and site personnel.
- All study teams involved and MEDSIR (Study Sponsor).

ESMO BREAST CANCER

Onsite and Online Congress

MEDSIR
MEDICA SCIENTIA INNOVATION RESEARCH

Torre Glòries, Av. Diagonal, 211 Planta 27
08018 Barcelona, Spain
medsir.org

INSTITUT
JULES BORDET

90, Rue Meylemeersch
1070 Bruxelles, Belgium

European Society for Medical Oncology (ESMO)
Via Ginevra 4, CH-6900 Lugano
T. +41 (0)91 973 19 00
esmo@esmo.org

esmo.org