5th International Workshop on PET in Lymphoma
Menton, September 19-20, 2014
PET adapted trials: The ongoing studies

OPTIMAL>60 (DSHNHL-2009-1, NCT01478542)
German High-Grade Non-Hodgkin's Lymphoma Study Group
PI: Michael Pfreundschuh, Homburg/Saar, Germany

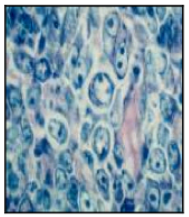
Dirk Hellwig

Speaker of the DSHNHL Nuclear Medicine Panel

Department of Nuclear Medicine

University Hospital Regensburg, Germany

German High-Grade Non-Hodgkin's Lymphoma Study Group



DEUTSCHE STUDIENGRUPPE HOCHMALIGNE NON-HODGKIN-LYMPHOME*

German High Grade Non-Hodgkin's Lymphoma Study Group

*(gefördert durch die Deutsche Krebshilfe)

Vorstand der DSHNHL: M. Pfreundschuh, Homburg, N. Schmitz, Hamburg, L. Trümper, Göttingen, M. Loeffler, Leipzig

- Network of oncologists and radiotherapists for large scale lymphoma trials
- About 150 peripheral centres in Germany
- Participated in several study generations
  - MINT
  - FLYER
  - RICOVER
  - ...
- Formerly no use of PET

Improvement of Outcome and Reduction of Toxicity in Elderly Patients with CD20^{+} Aggressive B-Cell Lymphoma by an Optimised Schedule of the Monoclonal Antibody Rituximab, Substitution of Conventional by Liposomal Vincristine, and FDG-PET based Reduction of Therapy in Combination with Vitamin D Substitution

Short title:

OPTIMAL>60 / DR. CHOP

DSHNHL 2009-1

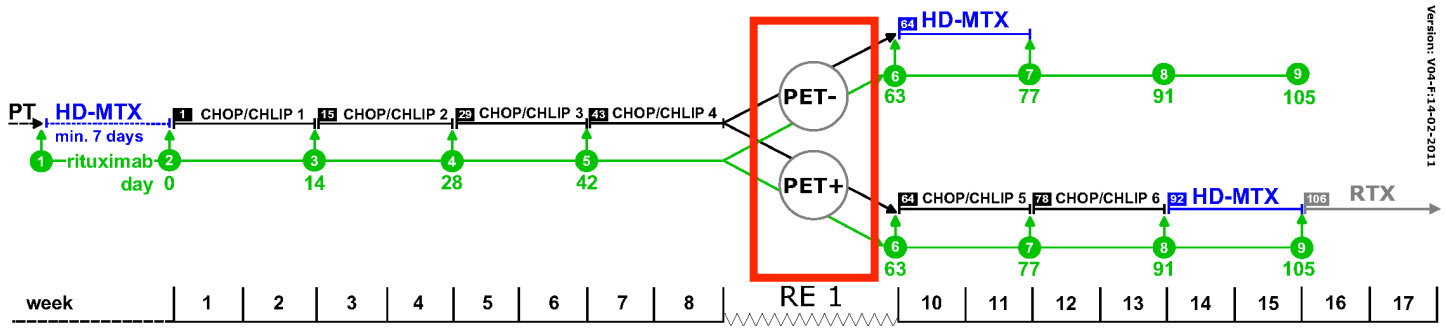
Date of Protocol:	12th of May, 2014
Status:	**approved by BfArM on 10th October 2011** **approved by the Ethics Committee of the Medical Council of Saarland on 12th December 2011** **Amendment 1: approved by the Ethics Committee of the Medical Council of Saarland on 3rd of July 2012** **Amendment 1: approved by BfArM on 4th of September 2012** **Amendment 2: approved by the Ethics Committee of the Medical Council of Saarland on 11th July 2012** **Amendment 2: approved by BfArM on 19th August 2014**
Version:	V05.0-F
EudraCT-No.	2010-019587-36
Protocol writing committee:	Prof. Dr. med. M. Pfreundschuh (author in charge)

Protocol synopsis of OPTIMAL>60

- Indication:
  - Elderly patients (61-80 years)
  - with aggressive CD20+ B-NHL
- Primary objectives of the study:
  - Less favourable prognosis:
    - To test whether progression-free survival (PFS) can be improved by substituting conventional by liposomal vincristine;
    - To test whether PFS can be improved by 12 optimised applications instead instead of 8 2-week applications of rituximab.
  - Favourable prognosis:
    - Comparison of neurotoxicity of conventional and liposomal vincristine;
    - Determination of PFS for the treatment strategy of reducing treatment in patients with negative FDG-PET after 4 x R-CHOP/CHLIP-14 (PET-4) and comparison with the corresponding patient population in RICOVER-60.

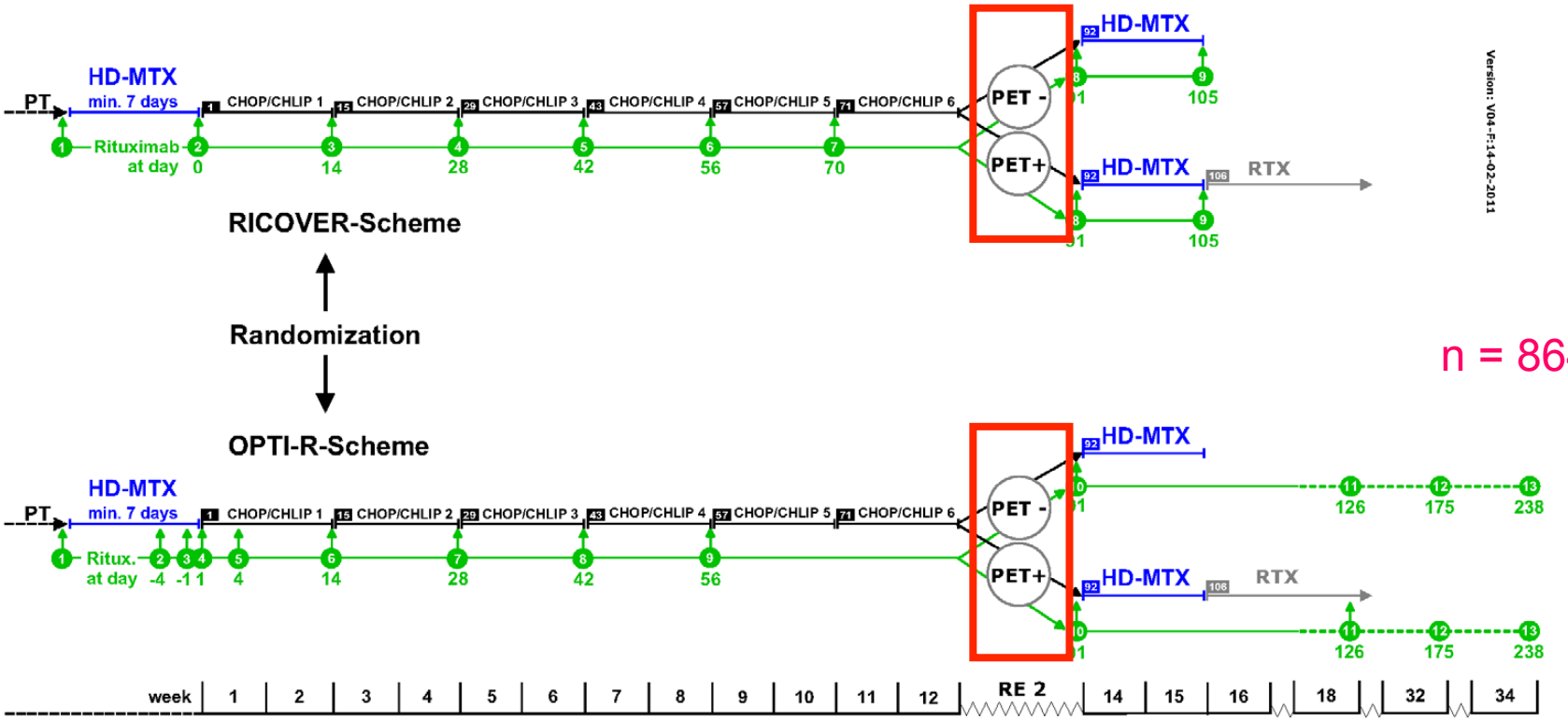
OPTIMAL>60 – Time schedule

Favourable prognosis



n = 288

Less favourable prognosis



n = 864

Note: HD-MTX only in patients with high risk for CNS disease

Protocol synopsis OPTIMAL>60

- Secondary objectives of the study:
  - Comparison of the prognostic value of a pre-treatment FDG-PET (PET-0) with conventional CT/MRT.
  - Investigation of the prognostic value of different FDG-PET derived imaging biomarkers for lymphoma load (SUV, MTV, TLG).
  - Comparison of the FDG-PET-based individualised treatment strategy in OPTIMAL>60 with the fixed (pre-defined) treatment strategy in RICOVER>60.
  - Estimation of the vincristine-related neurotoxicity ("OPTIMAL>60 Less Favourable only, since vincristine related neurotoxicity is primary objective of the study in favourable patients) and other toxicities (all patients).
  - Determination of the therapeutic efficacy of a vitamin D substitution by comparing the first patients without vitamin D substitution with patients with a vitamin D substitution.

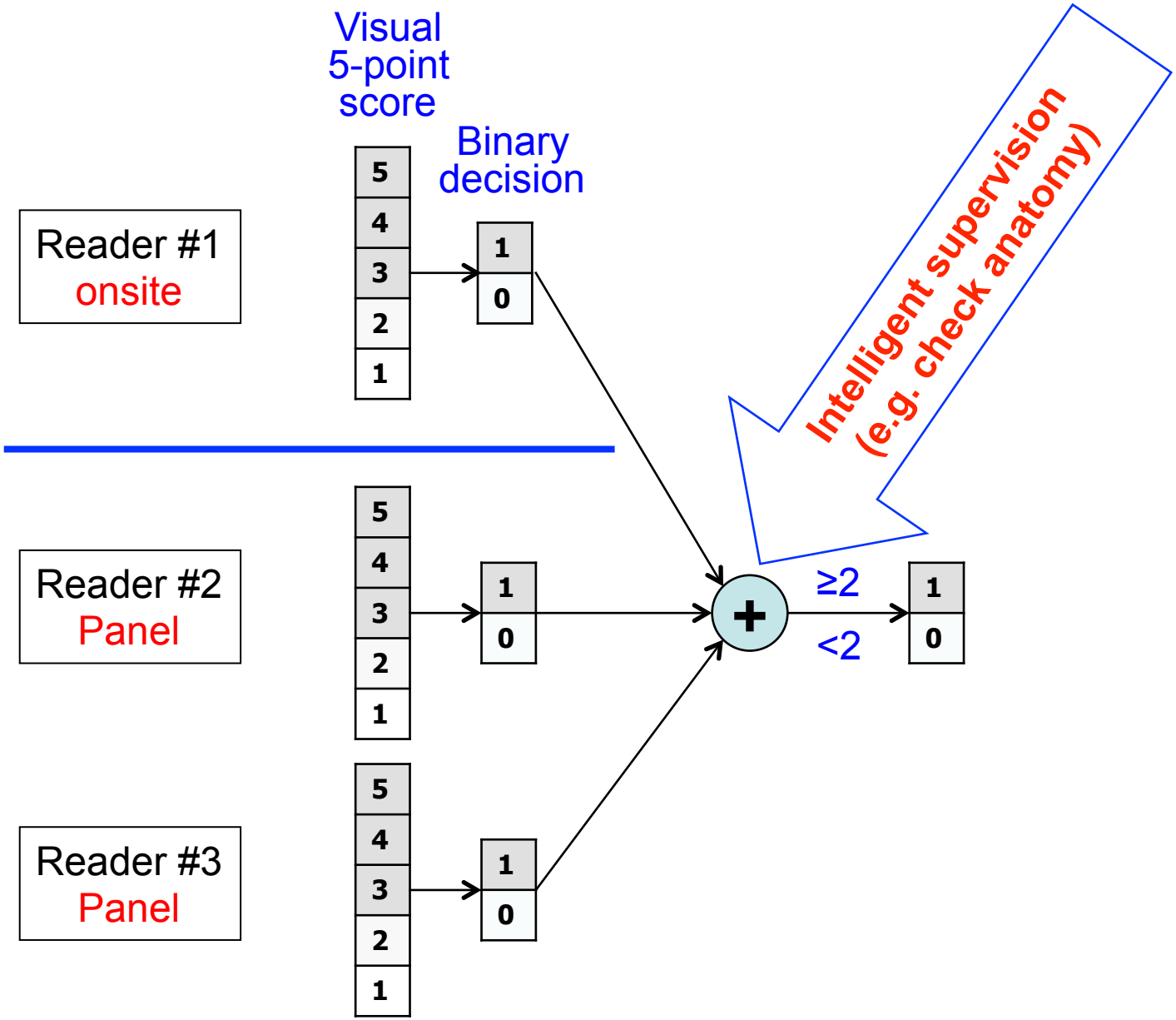
Special issues of PET in the OPTIMAL>60 trial

- PET not reimbursed in Germany
  - Support of the study concept by the Competence Centre Oncology of the Statuatory Health Insurances
- PET-0 (now mandatory)
  - But: Initial Ann Arbor stage not influenced by PET!
- Visual interpretation of restaging PET
  - Applicable even without PET-0
- PET is used for de-escalation
  - PET positivity related to mediastinal blood pool
- Collect all relevant imaging data
  - PET, CT, MRI from staging and response assessment

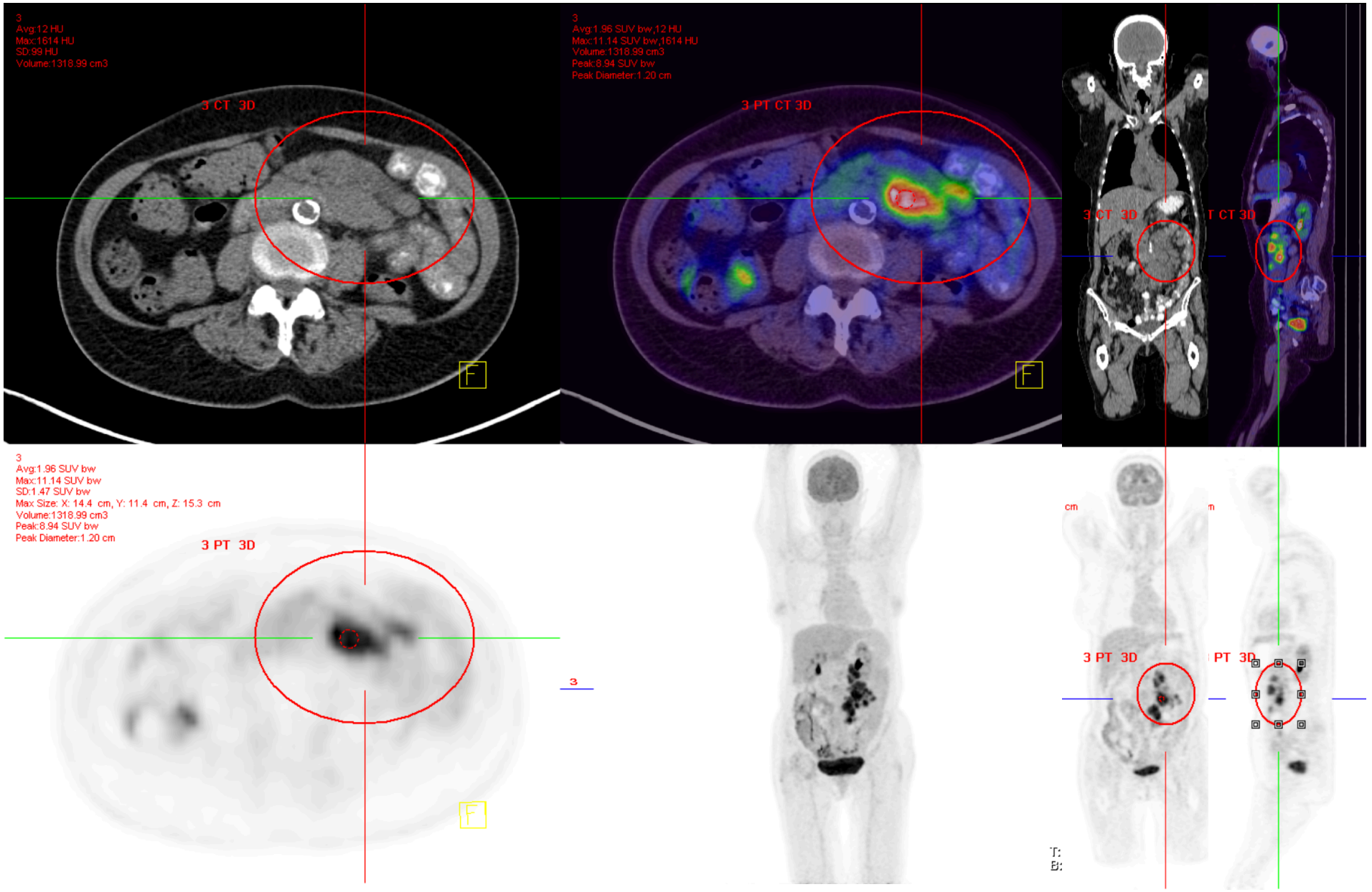
Storage concept and workflow

- Peripheral sites send DICOM images
  - Anonymized
  - DVD/CD
- Data server in Central Study Office
  - NAS + RAID system
- Email message to PET Reference Panel
  - 2 experienced PET readers
- Image analysis
  - Visual interpretation
  - SUV measurements if possible
- PET panel votum
  - Negative / positive

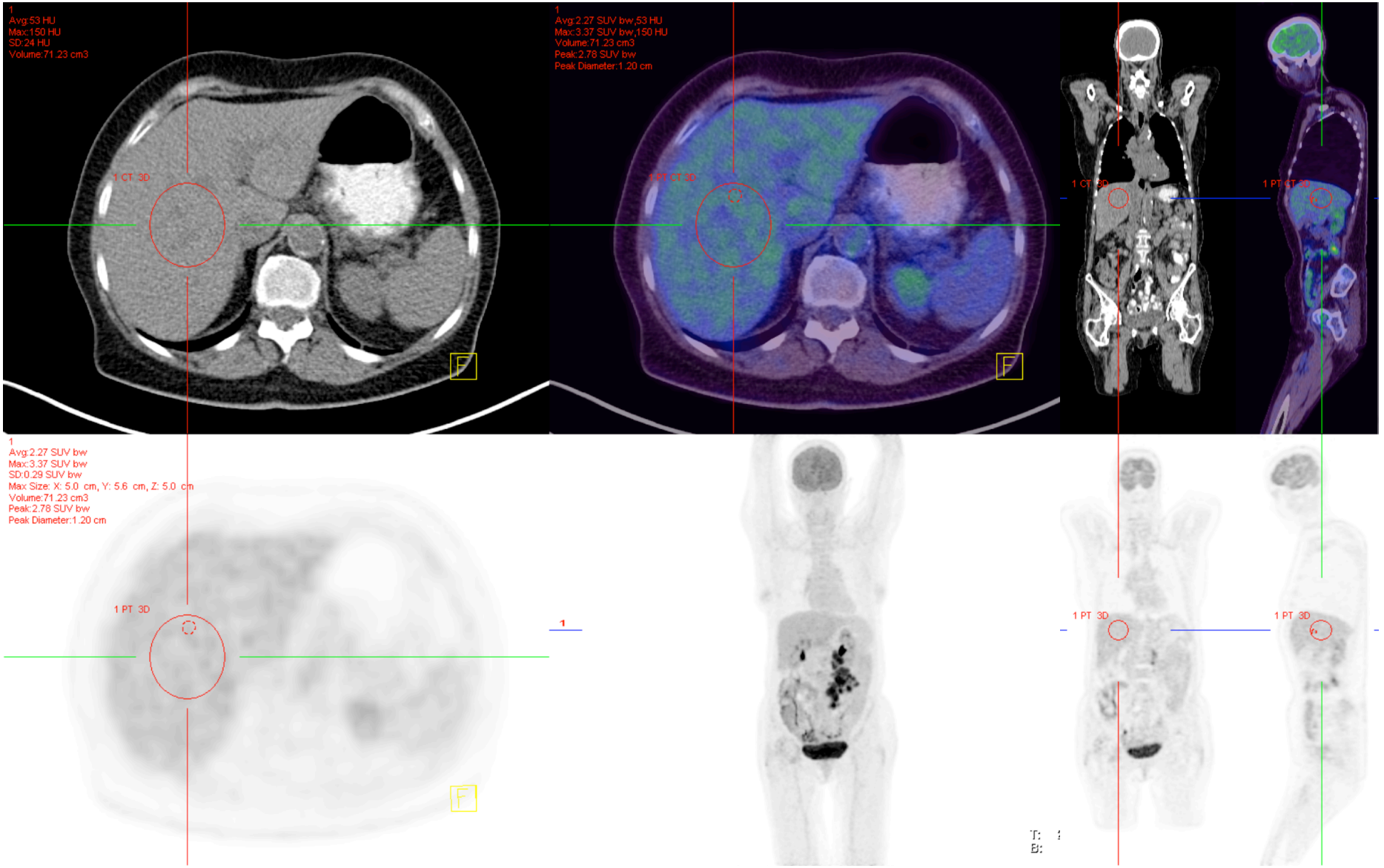
OPTIMAL>60: PET reading strategy



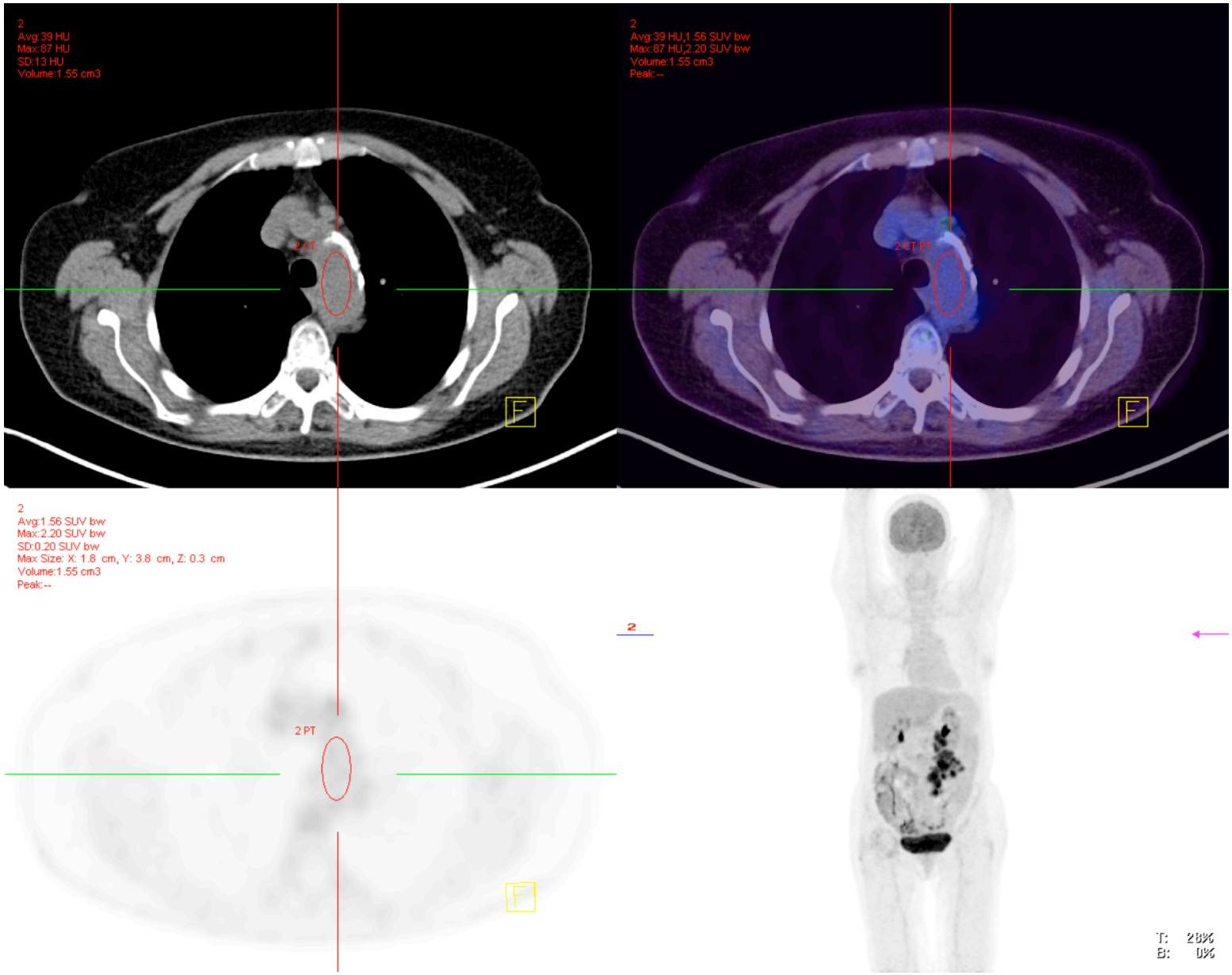
PET quantification: SUV Peak



PET reference region in liver: SUV Mean



PET reference region for mediastinal blood pool



PET/CT sites of the OPTIMAL>60 trial

- Time line:
  - Recruitment:
    11/2011 – 10/2016
  - Follow-up until 03/2020
- Current status
  as of 2014-09-15:
  - PET/CT centres:
    - 55 qualified
    - +12 from PETAL
  - Patient numbers:
    - N=366 randomized
    - N=284 restaged with PET
    - N=27 restaged without PET

▽ Central Study Office

▽ Reference Nuclear Medicine

Summary: OPTIMAL>60 trial

- FDG PET based de-escalation design with early termination of chemotherapy and omission of radiotherapy.
- Allows comparison with former DSHNHL trials to analyze potential benefit of PET usage.

- Well recruiting large scale trial with broad acceptance in the peripheral centres.
- Quickly established network of participating PET sites throughout Germany.
- Pragmatic workflow for collecting image data.

- Interim analysis results in early 2015.

Acknowledgement

- Participating centres from DSHNHL
- PETAL study group
  - S. Müller, U. Dührsen
- Colleagues from Cuneo, Italy
  - S. Chauvie, A. Gallamini, A. Biggi
- Competence Centre Oncology, MDK North Rhine of the Statuatory Health Insurances
  - A. Heyll, K.-P. Thiele
- Colleagues in the Central Study Office in Homburg/Saar, Germany
  - M. Pfreundschuh, G. Held, V. Pöschel, T. Rixecker, D. Ehlert