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European Organisation for Research and Treatment of Cancer
The future of cancer therapy

EORTC-STBSG
Study **1809 (STRASS 2)**

A randomized phase III study of neoadjuvant chemotherapy followed by surgery versus surgery alone for patient with High Risk RetroPeritoneal Sarcoma

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STRASS 2 main objective

- STRASS 2 aims to investigate whether patients affected by RPS with the highest metastatic risk (G3 DDLPS and LMS) could benefit from neoadjuvant chemotherapy.

- The main objective of this study is to demonstrate that neo-adjuvant chemotherapy, as an adjunct to curative intent en-block surgery can improve the prognosis of these patients by reducing the risk of development of distant metastasis.

Sub-studies

1) To evaluate the efficacy and safety of **Akynzeo** (netupitant + palonosetron) in the management of chemotherapy-induced nausea and vomiting in RPS patients receiving highly emetogenic chemotherapy regimens
   - Akynzeo is administered on D1 with dexamethasone
   - Helsinn proposes a d1/d3 regimen without dexa (experimental)
   - *Status*: Feasibility of sub-study being evaluated - contract/budget negotiations not started (Helsinn)

2) To demonstrate the clinical utility of **pro-gastrin** as a biomarker for disease burden and outcome in patients with sarcoma
   - Pro-gastrin is abnormally released in blood of pts with different types of cancer
   - Pro-gastrin assay (ELISA) exhibits high diagnostic accuracy for multiple cancers
   - *Status*: sub-study being developed – contract/budget negotiations not started (ECS progastrin)

Study organization

STRASS-2 is a multicenter phase III study run in 50 sites over 14 countries

STRASS-2 is an intergroup collaboration – EORTC STBSG is the leading group

- EORTC = sponsor in Europe
- SAKK = legal representative in Switzerland – *on hold due to COVID-19 until Sep 2020*
- CCTG = sponsor in Canada – *contract under discussion*
- ANZSA = sponsor in Australia – *contract under discussion*
- US = individual sites – *several aspects to be investigated (e.g. insurance,..)*

STRASS-2 is a fully academic study

- Confirmed support: Anti Cancer Funds (ACF) and ECRF
- National grant submissions ongoing
- Support from companies via sub-studies:
  - ongoing with Helsinn and ECS Progastrin

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Current status and timelines

- 2019 • **Outline v2.0 released**: 28-Jan-2019
- 2019 • **Protocol v1.0 released:** October 2019
- 2020 • **First REG submission:** May 2020
- 2020 • **CFR design and database ready**: June 2020 (Rave)
- 2020 • **First site active:** Sep/Oct 2020

Update countries:

Czech Republic: Submitted on 02/07 to CA and EC, no reply yet

Denmark: Not yet submitted to CA and EC

France: Submitted to CA and EC, Approval is expected soon (August)

Germany: Submissions are expected by end of August

Italy: Submissions to EC and CA are performed, Local ECs are evaluating the study

Netherlands: submissions are expected August

Poland: Submitted to EC and CA start of July

Slovakia: Submitted to EC and CA mid-June

Spain: EC approval received, CA approval expected next month

UK: CA approval is received, Packaged will be submitted soon to EC

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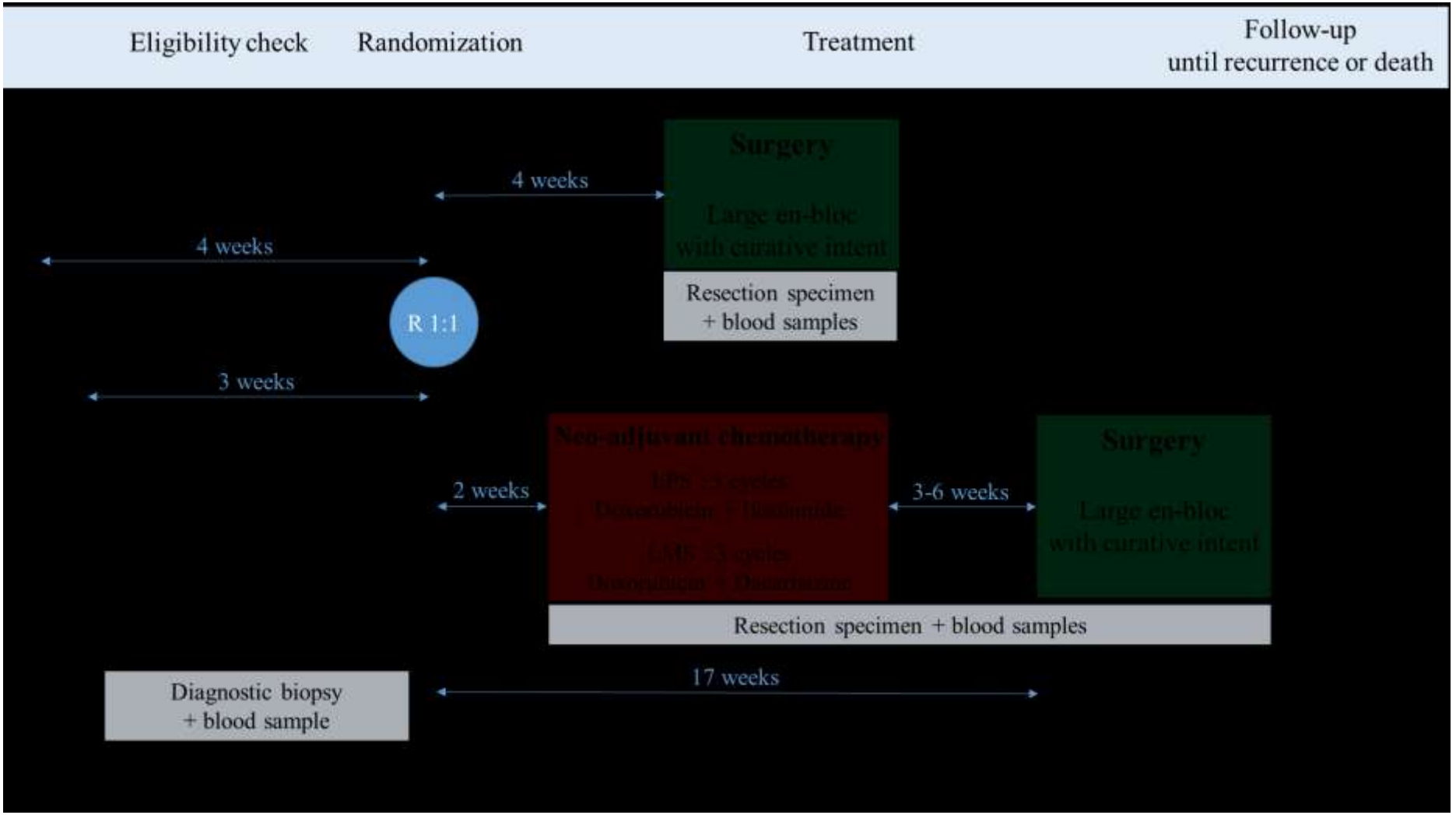
Study design



Endpoints

Primary endpoint: DFS including as events: distant PD on neoadjuvant treatment, local PD if not followed by R0/R1 surgery, non-operable tumors, distant metastases and/or local recurrence, R2 surgery, death.

Secondary endpoints:

- Overall survival
- Recurrence free survival
- Distant metastases free survival
- Cumulative incidence of local recurrences
- Cumulative incidence of distant metastases
- Radiological response to neoadjuvant chemotherapy according to RECIST
- Radiological response to neoadjuvant chemotherapy according to CHOI
- Pathological response
- Safety and toxicity of neoadjuvant chemotherapy
- Perioperative complications
- Late complications
- Health-Related Quality of Life

Study conduct

- 250 patients will be randomized over 66 months (5.5 years).
- follow-up = 1.5 years

- To ensure balance between the number of patients in the two histology cohorts, accrual to each cohort will be capped to 125 patients.

- Two interim looks for futility are foreseen in this design: one after approximately 40% of events have occurred (around 4 years after first patient in) and one after approximately 66.7% of events have occurred (around 5 years after first patient in)

Main eligibility criteria

- Histologically proven primary gr 2 or 3 LMS (>5cm) or gr 3 LPS (or gr 2 with no necrosis on biopsy, but clear necrosis on imaging) of retroperitoneal space or infra-peritoneal spaces of pelvis *
- Unifocal tumor
- No metastatic disease
- Resectable tumor: based on pre-op imaging performed within 28 days before randomization (R0/R1 expected)
- No previous surgery, RT or chemo for the present tumor

* Local histopathological diagnosis accepted for entry
FFPE collected for retrospective central histology review

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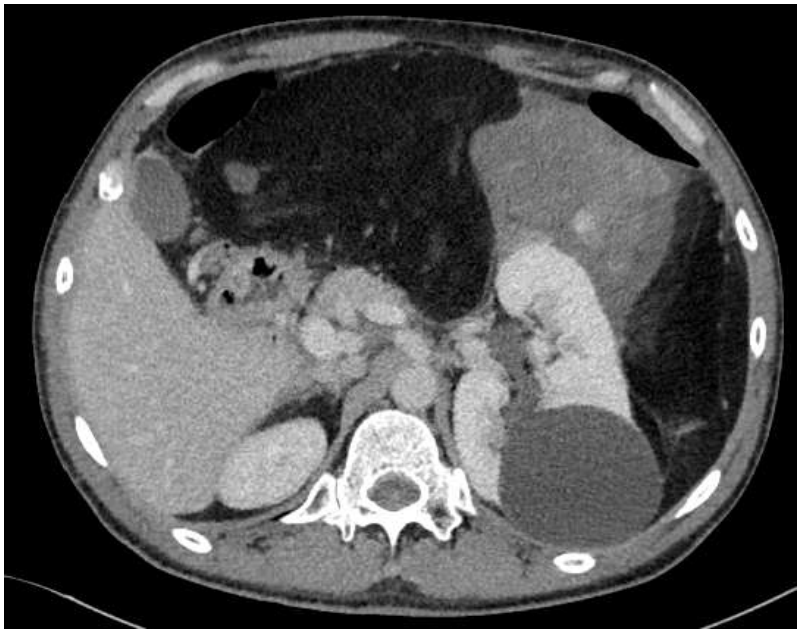
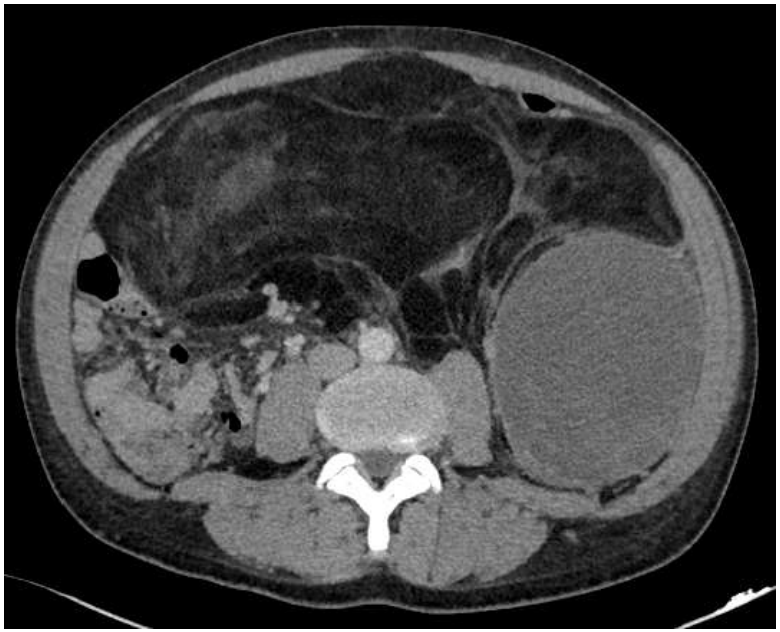
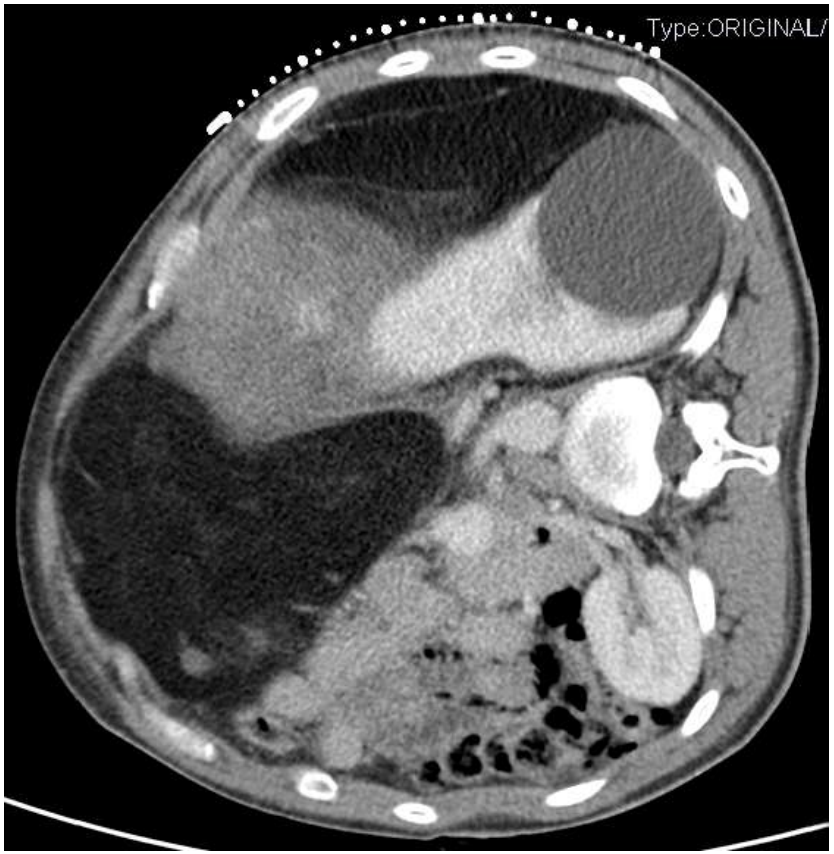
M 48 yrs



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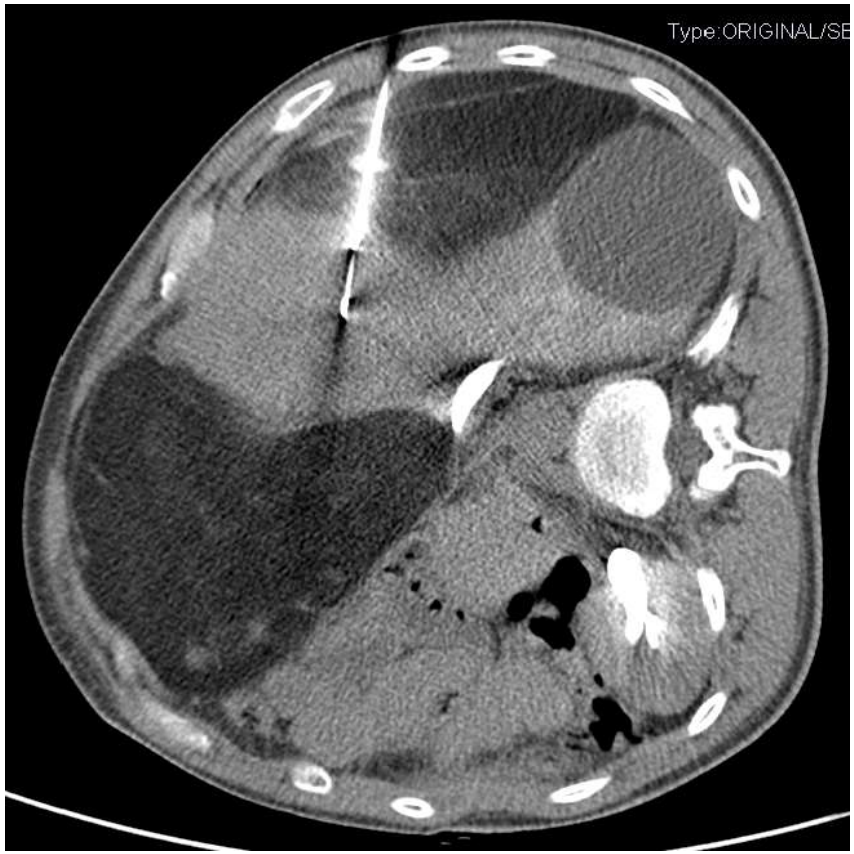
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G2 (D3,M1,N0) DD LPS

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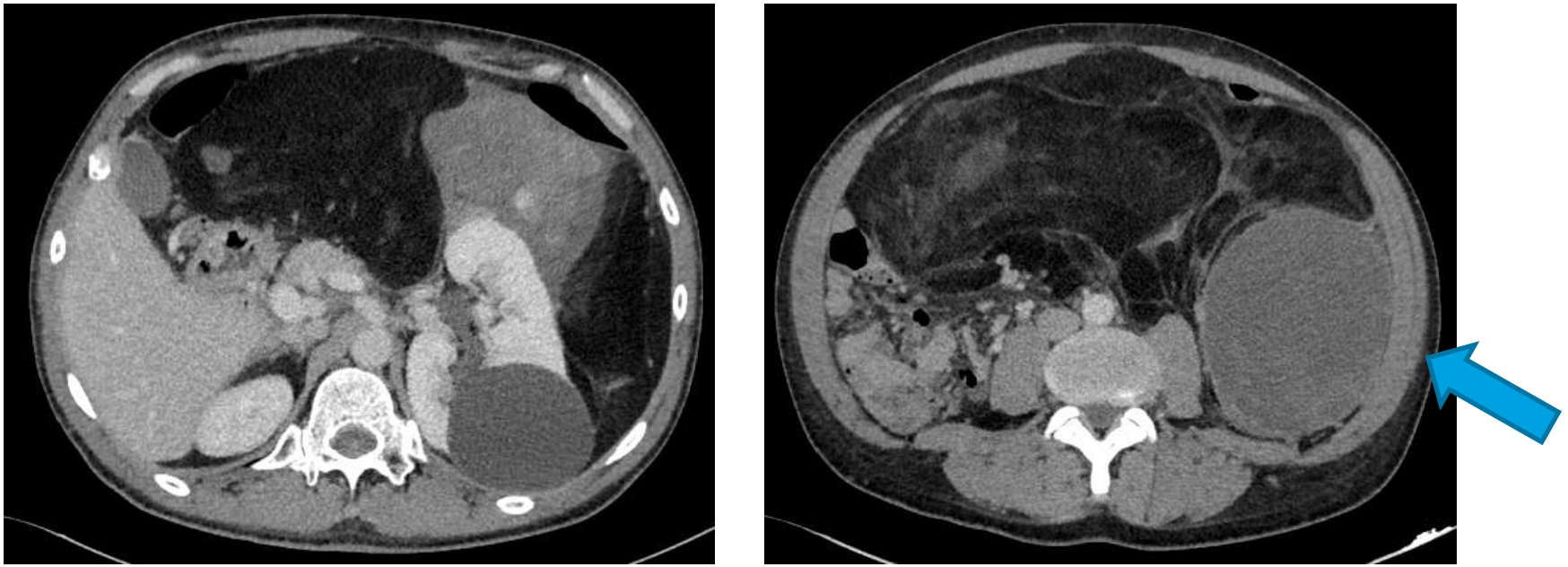

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G2 (D3,M1,N1) DD LPS

Necrosis <50% = 2

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- Unifocal tumor
- No metastatic disease
- Resectable tumor: based on pre-op imaging performed within 28 days before randomization (R0/R1 expected)
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Translational research

1) To identify molecular and immune-related characteristics relevant to response, correlate:
   - total mutational burden and treatment response / outcome
   - DNA repair mechanisms and drug resistance / tumour growth
   - methylation status and treatment response
   - ir

TR proposals are welcome from the group

2) To defi e with radiograp ION
   - estimate percentage of necrosis on initial imaging
   - predict the area of highest tumor grade

3) To use radiomic features extracted from CT and FDG PET/CT (optional) for prediction of tumor subtypes and clinical outcomes

4 diagnostic biopsies
(FFPE and FF samples)

Surgical specimen 2 tumor blocks + 1 healthy tissue
(FFPE and FF samples)

Blood
(baseline; pre-C2; pre-surgery; d15 post-surgery; at recurrence)

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Translational research

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Thank you!

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