TARPSWG Semiannual Meeting
Minutes

Wednesday March 13h, 2019, 2-6pm

Hilton Tokyo,
Ran room on the 3rd floor

Attendees to the meeting

Adamcova Krikorova Degmar, Ale Keiske, Almond Max, Asencio José Manuel, Bagaria Sanjay, Baldi Giacomo, Bemelmans Marc, Bonvalot Sylvie, Cader Sonia, Callegaro Dario, Cananzi Ferdinando, Cardona Ken, Caro-Sanchez Claudia Hayde, Caruso Denise, Catton Charles, Chen Jun, Chen Yen-Lin Evelyn, Chengua Luo, Covelli Andrea, D'Amato Gina, De Laney Thomas, Demicco Elizabeth, Devaud Nicolas, Dumitra Sinziana, Eckaray Mark, Engelen Sanne, Fairweather Mark, Farma Jeffrey, Ford Samuel, Garcia Ortega Dorian Yarih, Gervais Mai-Kim, Gladdy Rebecca, Goel Neha, Graham Danielle, Greer Jonathan, Grignani Giovanni, Grignol Valerie, Gronchi Alessandro, Gyorki David, Haas Rick, Hall Kristen S., Hanif Shahbaz, Hohenberger Peter, Hong Angela, Isubuchi Yuya, Iwata Shintaro, Jones Robin, Judson Ian, Kane John, Kasper Bernd, Kawai Akira, Kees Verhoef, Keisuke Ae, Keung Emily, Keymeulen Kristien, Kirsch David, Kirsh David Guy, Kollar Attila, Lahat Guy, Lam Miranda, Lee Kyo Won, Lim So-Hee, Loong Herbert, MacNeill Andrea, Mammen Joshua¸ Mann Gary, Martin Karla, Martins Pedro, Matsumine Akihiko, Mayo Skye, Meggison Hilary, Meyer Christian, Miao Chengli, Nessim Carolyn, Ng Deanna, Novak Marko, Ong Chu An Jonny, Pasquali Sandro, Pennacchioli Elisabetta, Purgina Bibianna, Quagliuolo Vittorio, Raut Chandrajit, Razak Albiruni, Roland Christina¸Roopavathana Beulah, Rutkowski Piotr, Sanfilippo Roberta, Sant Chawla, Sayyed Raza, Sbaraglia Marta, Schrage Yvonne, Sicklick Jason, Snow Hayden, Spraker Matt, Stacchiotti Silvia, Stoeckle Eberhard, Strauss Dirk, Swallow Carol, Takeuchi Akihiko, Trama Annalisa, Trent John, Tse Teresa, Tseng William, Van der Graaf Winette, Van Houdt Winan, Vassos Nikolaos, Vincenzi Bruno, Wagner Andrew, Wiseman Jason, Zaffaroni Facundo, Zaini Shane, Zih Francis.

Apologies

Akiyama Toru, Al-Refaie Waddah, Artigas Vicens, Brar Savtaj, Fiore Marco, Gelderblom Hans, Hayes Andrew, Howell Krisha, Jakob Jens, Kim Teresa, Lyons John, Maestro Roberta, Messiou Christina, Miah Aisha, Mullinax John, Nikisch Leandro, Perhavec Andraz, Pollock Raphael, Quildrian Sergio, Van Coevorden Frits, Wardelmann Eva

2:00-2:15pm: Welcome Introduction (A. Gronchi)

2:15-3:00pm: RESAR Update

- Update on Inclusion of patients with persistent disease, Recruitment, Sites and Funding (D. Gyorki).
    - RESAR on ClinicalTrials.gov (NCT03838718).
    - 28 sites active, 35 enrolling, 4 REB in progress.
    - 1220 patients so far (according to received updates to queries).
    - Upgrade of dataset: new fields added to enroll also patients with Persistent RPS after incomplete resection, as well as second previous/synchronous malignancies (all in- situ malignancies should be excluded).
        - ACTION: Patients with persistent disease can be enrolled in RESAR starting from Jan 1st 2020.
        - The new version of the database with added data will be distributed on the website.
        - In the past some centers were including residual disease and putting them in as an open biopsy followed by surgery. Now that we have these new data points we may have to retroactively correct these patients with the new data points or make a note of it when writing and analyzing data for future papers.
        - The first pooled analysis of data entered before 11/2019 and with a follow-up up to 03/2020 is going to be submitted to CTOS 2020.

- Are we collecting too much or too little data? Especially the data points about what was intended and what was done at the time of surgery. This will be analyzed and possibly simplified.

- Status of centralized RESAR data collection/registry (A. Trama).
  - Dr. Gronchi confirmed funding for database centralization.
  - Dr. Gyorki commented on the need for ensuring possibility of generating randomization sequences for patients included in the new platform.
  - The database will centralize data to ensure quality of data and prospective data monitoring.
  - The database will allow to export/import databases to/from different sources (e.g. File Maker, Excel and Red Cap).
  - An helpdesk will support support data transfer.
  - Reports will be available both for separate centers and all the centers.
  - The platform will have two data checks: 1) a logic check will be performed at each centre before sending in the data centrally and then 2) completeness of the data will be assessed centrally.
  - An agreement will be in place for data access, data analyses, authorship, DB functioning, Ethical and Privacy issues, consent form, and data sharing agreements.
  - Data centralization will need an amendment of the protocol to be uploaded locally. This is particularly important considering that RESAR will be the screening log for the STRASS-2 study.

  - ACTION: IT department will be working on setting up the platform in the next 5 months; a e pilot will be conducted afterwards.

- Data quality checks (C. Roland).
  - Issues discussed with Jeff Gershenwald and Lauren Haydu (MD Anderson, Huston, TX) for their experience with melanoma database:
    - need for a clear data dictionary;
    - data points that are absolutely necessary (minimum required data);
    - logic checks are needed (e.g. a WDLPS cannot have high malignancy grade);
    - dates should be all in the same metrics in an international DB (e.g. dd/mm/yyyy or mm/dd/yyyy);
    - A research project to start with can serve to test the database and demonstrate success.
    - A minimum of required data will be set up in order to have a small number of fields with strong data quality.
    - Data will be evaluated according to institution.

  - ACTION: A survey to RESAR participants to investigate their interpretation of the different data points in the data dictionary will be generated.

- Recommendation of new RESAR projects .
  - Complexity score project for post-op morbidity (M. Fairweather).
    - Plan for new census date for pooled projects – 30/11/19.
    - A surgical complexity score will be created with the available data points.
    - 26 centres agreed to participate, of whom 7 centers have already transmitted data for a total of 373 patients.
    - Issues with DTAs are generating delays at some institutions.
    - The deadline for data submission is of Jan 31, 2020.
    - We plan an abstract for CTOS 2020.

        - ACTION: Dr. Fairweather will start analyzing the first 373 patients to assess quality of data (e.g. quality and logic checks) and to ensure all of the necessary data points have been considered to complete this project.

    - Biopsy project (A. Gronchi).
        - A retrospective series from INT Milan and QEH Birmingham was analysed to investigate concordance of histopathological characteristics between preoperative biopsy and final pathology report revealing an overall good concordance. In particular specificity was high for high grade tumors (98%).
        - Here, the proposal is to look at accuracy with regards to grade between biopsy and surgical specimen within the Prospective RESAR database.
        - Differences in reporting histopathologic features at biopsy across RESAR centres can also represent a practice pattern question.
        - ACTION: Dr. Nessim will send out a call for participation for this project.

    - Correlation between anticipated extension of planned surgical resection and actual resection at surgery.
        - This study can be limited by inter-observer variability. However, the project is considered of interest by the participants of the meeting also to measures such variability.
        - ACTION: Dr. Gronchi to make proposal if still interested in this question.

    - Variation in pattern of care (H. Snow).
        - A study will investigate patterns of care for RPS patients with the aim of indentifying consistent patterns of care (i.e. "treatment agreement").
        - The study will investigate the following domains:
            - Diagnosis/Work up;
            - Neo-adjuvant treatments;
            - Extent of surgical resection.
        - Selection criteria:
            - Most frequent hisologies;
            - A minimum volume will be considered (i.e. < / > 13 RPS/year as per recent JACS paper):
        - Possible limitations due to variations in neoadjuvant therapies across centres.
        - The inclusion of recurrent tumours as well as primary tumours is to be discussed.
        - ACTION: Dr. Snow to submit a study proposal either through RESAR or as a retrospective paper if more likely to find all of the data points needed.

- Survey on the impact of STRASS on routine use of preop RT (C. Roland).
    - The results of STRASS study which have been presented in the abstract form have already been practice-changing at some institutions.
    - Surveying changes in clinical practice should be done after full-text publication of STRASS study.
    - The survey can be case-based.
    - At this stage, the survey should aim at investigating opinions of Medical Oncologists, Radiation Oncologists and Surgeons. This was agreed by the majority of the participants. A future survey should investigate the attitude of MDTs towards the results of the STRASS trial .
    - A pilot can be conducted also at this stage within the TARPSWG group.

- The Delphi model will be used.
- ACTION: Dr. Roland and Dr. Nessim will create the questionnaire with help from researchers specialized in Surveys at MD Anderson.

- Pathology guidelines consensus meeting (E. Demicco).
  - The following issues were presented:
    - Processing of the surgical specimens;
    - Standardization of surgical specimen processing and pathology report;
    - Analysis of tumour necrosis and surgical margins.

  - ACTION: Each institution should ask their pathologists if they are interested to be part of a working group to develop a consensus.

3:00-3.30pm: Update Consensus guidelines on primary RPS (C. Swallow – D. Strauss).

- The guidelines are now about 5 years old and need to be revised, particularly as they are widely diffused and used with an impact on clinical practice.
- Two main things have changed since the last publications:
  - Histology specific outcomes:
    - Guidelines stated that negative microscopic margins are needed for LPS; currently it is agreed that WDLPS and DDLPS should only have a macroscopic negative margin while LMS, SFT, and MPNST needs a microscopic negative margin;
    - A statement should be added for a planned positive margin, when patient's clinical condition and co-morbidities are considered;
    - Revised guidelines on percutaneous biopsy should report that not only trans-retroperitoneal approach is to be used (current version) but also trans-abdominal approach, providing that the needle is sheathed and a co-axial technique used by interventional radiology.

  - STRASS:
    - The morbidity with IMRT is acceptable;
    - A summary of findings already reported has been presented, including:
      - When all sub-types were analysed, no impact on local control and OS when surgery is done at an expert center;
      - A non-statistical significant advantage was identified for WDLPS;
      - Patients with high grade 3 LPS and LMS did not seem to benefit from Pre-operative Radiotherapy alone;
    - These findings highlight the importance of analysing high grade tumours in STRASS 2;
    - A summary statement should be considered in guidelines about these findings and their impact on the decision making process.
    - Participants are willing to consider a randomised study for radiation therapy for G1 and G2 retroperitoneal liposarcoma.

  - ACTION: TARPSWG members will receive guidelines and must respond on the consensus statement within 2 weeks of receiving it to be an author.

3:30-3:50pm: Dynamic prediction in primary RPS (D. Callegaro).

- This study was a spinoff project of STREXIT.

- The study generated a dynamic prognostic nomogram for RPS survivors.
- The Paper was accepted and was added to the Sarculator App.
- Future studies will consider:
    - asking the patients about having this information;
    - a clinical trial comparing a sarculator-personalized and a standard follow-up schedule;
    - investigating predictive implications of Sarculator predictions.

3:50-4:20pm: Strass vs Strexit projects (C. Raut – A. Gronchi).

- STREXIT analysed data of patients who were eligible for the STRASS trial and eventually were not randomised at the largest study centres (10/31 centres which enrolled up to 70% of the study patients).
- Study analysis showed a significant role for the surgeon in charge of the patient for the decision of not being randomised in STRASS despite being eligible.
- A manuscript is in progress.
- A study comparing patients who enrolled in STRASS and those who were not enrolled is planned to investigate the following outcomes: 1) Abdominal recurrence free survival; 2) Local recurrence and distant mets.
- An analysis is also planned to investigate the role of radiation therapy in the STREXIT cohort using a propensity score approach ad accounting for different histologies with particular regard to WDLPS and DDLPS.
- An analysis on safety of radiation will be conducted.
- An analysis on Surgical Quality and Center Volume will be conducted .
- An analysis on Morbidity and Quality of Life will be conducted.

- <u>ACTION</u>: In order to assess the quality of the data in the Prospective STRASS Registry the RESAR database can be exploited to evaluate the quality of the data points.

4:20-4:30pm: Post-nephrectomy outcomes project (M. Fairweather).

- This study gathered together 701 patients (500 patients had nephrectomy) who underwent surgery at three centres: Brigham, Milan, and Mount Sinai.
- Multiple time points of Creat/eGFR were analysed.
- Median follow up was 37 months.
- Main study findings include: 1) when EGFR was <60, 7 years after surgery were need to recover a normal EGFR; 2) 16% of patients developed new CKD stage 3 or more; 3) 2.5% of patients required dialysis; 4) Age>60 was the only independent predictor of CKD.
- <u>ACTION:</u> New studies on this topic were considered. A possible study should look at HFX tolerance when one kidney is left.

4:30-5:00pm: REC Committee Update (C. Nessim).

- Reviewed all projects currently that have succeeded, in progress and upcoming.

- COMPLETED PPROJECTS
    - Schwannoma Project.
    - Recurrent RPS Nomogram.
    - Whipple procedure in RPS.
    - Post-operative morbidity after resection of a primary sarcoma (Series: 1,007 patients).
    - Risk of recurrence after resection of a primary sarcoma (Series: 1,007 patients).
    - Guidelines for primary RPS (now updating it).

- Guidelines for recurrent RPS.
- Guidelines for metastatic RPS.

- PROJECTS IN PROGRESS
  - Presentation of Left Pancreatectomy project (S. Bagaria).
    - The study included 26 centers.
    - The study period was 10 years.
    - Analysis were conducted on 2,183 Primary RPS. There were 955 left sided RPS (43%), of them 278 (29%) had distal pancreatectomy.
    - Pathology reports showed that the pancreas invaded in 38% of cases.
    - Pancreatic fistula was B and C in 19% and 5% of patients, respectively.
    - Investigated factors were not statistically significant associated to POF. In particular, preoperative radiation, use of somatostatin analogues, mode of pancreatic division (staplers, sealants, or tissue flaps), level of pancreatic division (neck, body, tail), and use of drains did not predict POPF.
    - An abstract was submitted to SSO 2020 in Boston.

  - Presentation of Neo-Adjuvant Chemo project (W. Tseng)
    - This study analysed a matched cohort of patients who underwent surgery between 2008 and 2018 from 8 centers .
    - The main study aim was to compare RPS objective response to chemothearpy.
    - 121 patients had chemotherapy. There were 23 partial response.
    - Tumour response was more likely when more cycles were administered. This is likely the result of a selection bias, with responding patients being given more chemotherapy cycles.
    - Interestingly, PR were higher with DTIC in LMS.
    - No statistically significant difference was detected according to chemotherapy regimen in G3 DDLPS.
    - OS did not differ in the mat
    - An abstract has been selected at CTOS 2019, Tokyo.
    - ACTION: The DTA with all centres has to be finalise in order to do the final analysis and writing the manuscript.

  - Presentation of the Primary Mesenteric Sarcoma Project (S. Ford).
    - The study included 15 centers, with an average 3-4 patient/center.
    - Analysis will be performed.

  - Presentation of the Myxoid LPS project (C. Nessim).
    - The study data set includes 47 Primary Retroperitoneal MLS and 1,000 Extremity MLS.
    - Preliminary findings show longer OS, DFS, and lower incidence of LR for MLPS seated in the extremities compared to those seated in the retroperitoneum.

    - ACTION: The participating centres will be contacted and asked to perform molecular confirmation of MLPS. Also, tumour location will be carefully re-examined checking whether the tumour was in the psoas muscle or if it was truly in the retroperitoneum

  - UPCOMING PROJECTS:

- Surveillance post-surgery for Sarcoma (S. Ford).
  - SF received a grant to come to Ottawa to design a pragmatic trial on Imaging Surveillance post-surgery in Sarcoma.
  - The study endpoints will be DFS and OS.

  - ACTION: If anyone interested to participate, they should contact Dr. Ford

- Proposal Ganglioneuroma project (J. Siclick):
  - New proposal for a natural history project on ganglioneuroma.

  - ACTION: Dr. Siclick to submit proposal to REC.

- PELVISARC
  - New proposal will be circulated to the group next week calling for participation into this project.

5:00-5:30pm: Recurrent RPS series:

- Morbidity post resection of recurrence (G. Lahat):
  - The need for blood transfusion was the only independent predictive factor of post operative morbidity.
  - The occurrence of severe complications was not associated to either OS, or DFS, or DM.
  - An abstract has been selected at CTOS 2019, Tokyo.
  - The manuscript is in progress.

- Outcomes of patients after a second recurrence (R. Gladdy).
  - 400 patients recurred (81% had a local recurrence, 14% had distant recurrence).
  - Patients who had surgery did better.
  - Longer disease-free interval, lower grade and histologic subtype were associated to better outcomes.
  - Interestingly, patients with DDLPS often had both local and distant recurrence at the same time, leading to the worst outcome.
  - An abstract has been selected at CTOS 2019, Tokyo.
  - The manuscript is in progress.

- Change in Grade between the primary and the recurrence (C Nessim and S Bagaria).
  - In 20% of patients who had recurrent disease, tumour malignancy grade did worsen between the primary and the recurrence.
  - Patients who experienced grade worsening grade had sorter DFS, mainly for a shorter time to local recurrence.
  - OS was not statistically different between patients who had same grade and worse grade at recurrence.
  - An abstract has been selected at SSO 2020 in Boston.

- Any new recommendations of ideas for this dataset?
  - ACTION: Research hypothesis for new studies should be submit to Dr. Gronchi or Dr. Raut.

5:30-5:50pm: Update STRASS 2 (W. vanHoudt)

- The study will address the following outcomes:
    - Prognostic outcome (DFS primary end-point; OS secondary endpoint);
    - Quality of Life;
    - Imaging studies;
    - Translational endpoints.
- The study sites will be identified by EORTC.
- CCTG in Canada has approved the study with funding.
- ANZSA in Australia has endorsed the study waiting for funding.
- US has endorsed the study waiting for funding.
- SAKK waiting for endorsement.
- Study budget is 1.7 million (excluding imaging, translational and QoL studies).
- The study secured 400 000 Euros plus 1 million Euros by EORTC.
- The study protocol was approved two weeks ago.
- The first study site will likely be active in April 2020.
- Of note, it will not be mandatory to be part of RESAR to enroll into STRASS 2.

5:50-6:00pm: TARPSWG: time to brainstorm beyond RPS? (All) Should we expand to abdominal wall and extremity sarcoma? This will be discussed further

6:00pm: AOB and adjournment (A. Gronchi)