TARPSWG MEETING MINUTES
Rome, Nov 15, 2018

Attendants: Safia Ahmed, Toru Akiyama, Markus Albertsmeier, Max Almond, Eisar Al-Sukhni, Mohammad Alyami, Sanjay P Bagaria, Giacomo Giulio Baldi, Elizabeth Baldini, Marc Bemelmans, Andrew Bishop, Jean-Yves Blay, Sylvie Bonvalot, Savtaj Brar, Monica Brenca, Ferdinando Cananzi, Kenneth Cardona, Claudia Caro, Charles Catton, Tom Wei-Wu Chen, Luo Cheng Hua, Andrea Covelli, Antonino De Paoli, Angelo P. Dei Tos, Tom Delaney, Sinziana Dumitra, Makoto Endo, Mark Fairwhethear, Marco Fiore, Michael Folkert, Samuel Ford, Annamaria Frezza, AJ Hans Gelderblom, Maikim Gervais, Rebecca Gladdy, Ricardo Gonzalez, Josè González, Giovanni Grignani, Valerie Grignol, Alessandro Gronchi, Abha Gupta, Rick Haas, Amy Hayden, Ilkka Heiskannen, Peter Hohenberger, Angela Hong, Charles Honoré, Krisha Howell, Shintaro Iwata, Jens Jakob, Daniel Jordão, Ian Judson, John Kane, Bernd Kasper, Akira Kawai, Emily Keung, Kristien Keymeulen, Theresa Kim, Hirushi Kobayashi, Thomas Kraus, Miranda Lam, Axel Le Cesne, Lars Lindner, Herbert Loong, Heather Lyu, Andrea MacNeill, Aiko Maejima, Roberta Maestro, Gary Mann, Andrea Marrari, Karla Martin, Pedro Martins, Martin McCarter, Pierre Meeus, Nikolaos Memos, Alessia Mondello, Augusto Moreira, Carlo Morosi, John Mullinax, Micheal Nathenson, Federico Navarria, Carolyne Nessim, Deanna Ng, Marko Novak, Elena Palassini, Emanuela Palmerini, Sandro Pasquali, Shreyaskumar Patel, Elisabetta Pennacchioli, Ivy Peterson, Raphael Pollock, Bibianna Purgina, Shawki Qasim, Vittorio Quagliuolo, Sergio Damián Quildrian, Marco Rastrelli, Chandrajit Raut, Paul Ridgway, Evelyne Roets, Lorella Rusi, Piotr Rutkowski, Sergio Sandrucci, Roberta Sanfilippo, Marta Sbaraglia, Yvonne Schrage, César Serrano, Jason Sicklick, Silvia Stacchiotti, Eberhard Stoeckle, Dirk Strauss, Kim Sung Joo, Carol Swallow, William Tseng, Dimitri Tzanis, Sergio Valeri, Claudia Valverde, Frits Van Coevorden, Winette Van der Graaf, Jos van der Hage, Winan Van Houdt, Kees Verhoef, Andrew Wagner, Micheal Wagner, Jiping Wang, Eva Wardelmann, Jusuf Wirawan

Apologizes: Samuel Aguiar, Nita Ahuja, Waddah B. Al-Refaie, Sally Burtenshaw, Dario Callegaro, Peter Chong, David Gyorki, Andrew Hayes, Fabian Johnston, Christina Lynn Roland, John Lyons, John T Mullen, Venu G Pillarisetty, Martha Quinn, Myles Smith

1. RESAR UPDATE

A) Dr. Marco Fiore updated the group on data collection and status of RESAR
   a. 22 Sites are currently recruiting patients, 580 patients in 1.5 years
   b. 3 more have IRB accepted
   c. 1 more have submitted IRB
   d. 15 new centers interested

   ACTION: For other centers interested to join the study, please contact tarpswg@gmail.com; documentation for IRB submission is available on the website (www.tarpswg.org) / password protected, please ask for information to Marco Fiore

   e. www.tarpswg.org website is going well.

   ACTION: If you would like to have your profile on the website, or you would like to volunteer for website updates/master then please contact Marco Fiore (marco.fiore@istitutotumori.mi.it)

B) Dr. Dirk Strauss highlighted what studies could potentially be the first analysis of RESAR and to ensure the clinical questions being asked have the potential to help or change practice and be meaningful to practice.
The proposal is that the data collected in the RESAR database at each site should be pooled with a census date of 01 Jan 2019 (2 years of enrolment). This is an opt in study: if sites that are collecting data for RESAR do not wish to participate in this study, they do not need to share their data. Data will be collected in Milan: data transfer agreement will be shared for each participating site.

Several ideas for first analysis of RESAR data.

a. Creation of a primary RPS surgical complexity score based on patient, operative, and tumor factors that can be used to predict morbidity.
b. Predictors of impaired postop renal function after nephrectomy
c. Perioperative complications
d. Correlation of preoperative radiographic findings with preoperative and intraoperative decision making and histological organ invasion / Does a discrepancy between preoperative plan and operative outcome predict for worse outcome?
e. Extent and rate of organ invasion by histotype
f. ERAS vs no-ERAS (not currently collected in the RESAR data) –
g. Geographic differences in approach - could look at institutional differences eg case volume, epidural use - and then do a stratification by complexity score from 1.

ACTION: The group as a whole agreed that we should start with the Surgical Complexity Score project, and this would be led by Dr. Mark Fairweather at BWH-DFCI.

C) Dr. Mark Fairweather discussed the possibility of simplifying data entry as there are many data points to collect on each patient and this is quite time consuming.

He showed how dropdowns in clinical notes using **EPIC** (if your center has EPIC) could have all the information upload directly into the DATABASE

a. For those centers that have EPIC, Dana Farber can share their already created drop downs for Surgery, Medical Oncology, Radiation Oncology etc. They are continuing to work on this effort
b. This would reduce costs as well as you would not need a data entry person in your center and would save a significant amount of time

ACTION: for more information on using EPIC contact Mark Fairweather and Heather Liu at Dana Farber

D) Dr. Alessandro Gronchi discussed the hypothesis of centralization of the data in one database. Some funding may have been secured for this in Milan (confirmation expected in late December): in case of positive feedback, this grant would allow for 3-5 years operational costs of centralization and data monitoring from Milan. Dr. Gronchi will update the Group on this.

ACTION: the Group agreed to centralize the data collection in Milan

E) Dr. Sylvie Bonvolat made the proposal to include patients referred with gross residual primary disease after incomplete surgery into the RESAR database; other members proposed to include patients with locally recurrent disease.

The Group as a whole agrees to start collecting data on residual primary RPS undergoing completion surgery. Recurrent RPS, on the contrary, will not be included in RESAR at the moment

ACTION: the dataset will need to be modified, in order to catch information regarding the type of patient (primary vs residual primary) and not to allow double inclusion of the same patient by different institutions. Dr. Marco Fiore is appointed to modified the dataset.

2. <u>REC (Research Evaluation Commitee) Update:</u>

Dr. Carolyn Nessim reviewed the REC over the last 8 months.

a) There are 7 members on the committee now
b) Six new studies proposal are available at the moment
    1. Neo-adjuvant Chemo study (Will Tseng)
    2. Distal Pancreatectomy study (Sanjay Bagaria)
    3. Myxoid Liposarcoma study (Carolyn Nessim)
    4. Mesenteric Sarcoma study (Sam Ford)
    5. PelviSarc study (Marco Fiore)
    6. High Volume Sarcoma center study (Waddah Al-Rafaie)
c) The concept of Surveys to be circulated to the Group for academic purposes has been discussed.
    The Group agrees that surveys are circulated, provided that:
    a. They are reviewed by the REC and approved before sending out the whole group
    b. Aim of the survey is made clear (for research and publication vs. just for local information)
    c. Identify specialty of the person answering the survey as well as the institution in order to avoid overlapping data
    d. A maximum number of surveys should be sent out per year.

    ACTION: The REC committee will decide on a reasonable number of surveys per year and will take care of surveys selection

3. <u>STREXIT</u>

Dr. Carol Swallow presented the STREXIT data.

a) Significant variability by center in offering STRASS trial to eligible patients
b) Reason not to include patients was often "Surgeon preference"
c) Data on improved outcome per time for STREXIT patients will be presented at SSO
d) Data on survival outcome for STREXIT patients will be compared to outcome of STRASS patients in the future, after STRASS study publication

ACTION: If new center would like to join STREXIT study, please contatct Dr. Swallow. Requisites: at least 1 patients enrolled in STRASS; institutional prospectively maintained database of operated primary RPS. Deadline: end December 2018.

4. <u>STRASS2</u>

Dr. Winan van Houdt discussed the STRASS2 Protocol proposal. This is an EORTC led randomized clinical trial comparing neo-adjuvant chemotherapy for LMS and G3DDLPS retroperitoneal sarcoma, versus surgery alone.

- Phase lll superiority study
- 250 patients to be randomized
- Study duration
  - Recruitment: **5.5 years**
  - FU: **1.5 years**
- Two interim analyses for futility approx. 4 and 5 years after randomization

Primary endpoint:

Disease free survival (from registration) will include all events progression on neoadjuvant treatment, non-operable tumors, distant metastases and/or local recurrence.

Secondary endpoints:

- Radiological response at early evaluation (post-C1) and time of surgery (post-C3)
- Pathological response
- Recurrence free survival
- Overall survival
- Metastases-free survival
- Safety and toxicity of neoadjuvant chemotherapy
- Perioperative complications
- Late complications
- Health-Related Quality of life (EORTC QLQ-C30)

Inclusion criteria:

Primary liposarcoma (LPS) or leiomyosarcoma (LMS) of retroperitoneal space or infra-peritoneal spaces of pelvis.

- All grades of LMS can be included (grade 2-3)
- All grade 3 DDLPS can be included.
- DDLPS with confirmed grade 2 on biopsy can be included when:
  - The tumors carry a high risk gene profile as determined with Complexity INdex in SARComas (CINSARC-high)(4)
  - Confirmed grade 2 DDLPS with FNCLCC score =5 have no necrosis in the biopsy, but clear necrosis on imaging.

Statistical design:

- null hypothesis including estimate for control group: DFS at 3 years of 36.3%
- alternative hypothesis as used for the power calculation: DFS at 3 years of 54.4%, equivalent to a HR = 0.6

RESAR will be used as a registry cohort to compare the outcome of these patients with the outcome of a registry cohort of patients for whom surgery +/- pre-operative chemotherapy could have been considered but for whom the eligibility criteria were too restrictive or patients did not want to be randomized, to see how the outcome of the randomized patients compares with real-life, clinical practice data. RESAR database will be kept outside and independent of the study and the study budget.

The study proposal has been thoroughly discussed within the Group, with the following main comments:

a) Biopsy results in DDLPS may underestimate grade 3 tumours
b) Re-evalutation after only one cycle of chemotherapy may be too early for most medical oncologists
c) Include a stopping rule for safety if an excessive number of patients will progress during neo-adjuvant CT
d) Correlative Studies and TR were discussed: imaging with PET CT or PET MRI to predict response; translational research with NGS, Immunoprofiles etc. These correlative studies would require funding and could be led by another center
e) A suggestion to include a Medical Oncologist within Study Coordinators has been made

ACTION: A survey will be sent out to the group asking to each site what they are capable of doing and to confirm interest in joining STRASS2

5. <u>Recurrent RPS Project:</u>

Dr. Chan Raut gave on update on the Recurrent Sarcoma Project

a. The Recurrent Nomogram has been resubmitted for publication to *Clinical Cancer Research*
b. Nomogram validation has been attempted, but still some problems are encountered due to short follow up and missing data
c. Other studies that may be conducted on the collected data include:
    - Morbidity post resection of recurrence
    - Outcomes of patients after a second/third resection of a recurrence
    - Change in Grade between the primary and the recurrence

6. <u>Radiation Therapy Substudy on first paper on 1007 pts with RPS:</u>

Dr. Rick Haas presented on the outcome for Radiation Therapy on the original 1007 patients cohort, analysis the liposarcoma sub-population (60 patients):

234 WDLPS	RT+S 11.8%	S alone 39.2%	p 0.011
242 DDLPS GI-II	RT+S 29.0%	S alone 56.7%	p 0.008
131 DDLPS G III	RT+S 29.8%	S alone 43.7%	p 0.025

Effect of RT was lost in all subgroups after IPTW analysis.
Paper accepted for publication in *Cancer*

7. <u>Chemotherapy Substudy on first paper on 1007 pts with RPS:</u>

Dr. Charles Honoré presented the stusy on chemotherapy on the original 1007 patients cohort with primary sarcoma. Based on the data of these patients they have created a propensity score for the benefit of neo-adjuvant or adjuvant chemotherapy in RPS. Analysis to come.

8. <u>TARPSWG Governance:</u>

Dr. Alessandro Gronchi acknowledge the great progress that over the last 5 years the Working Group has obtained, based on a voluntary, friendly and enthusiastic fashion. The Group has progressively enlarged, and maybe time has come to formalize a governance structure for the activities of the Group.
Dr. Gronchi also announced that a proposal will be done to CTOS Board of Director to ask the Society to formally endorse the Working Group.

The Group discuss with several comments on this:

- Most agreed that membership will be allow to all who wants to join. No inclination to turn this into a society with membership fees is felt by most participants.
- Consider to change the name of the group to include Australia and Asia, considered the growing participation.

ACTION: a proposal to change the name into "Transatlantic Australasian RetroPeritoneal Sarcoma Working Group (TARPSWG)" is done by Dr. Strauss, Dr. Gronchi, Dr. Raut, Dr. Fiore. This will allow to keep the acronym unchanged, in order to preserved it as already indexed in PubMed from previous publications from the Group. A formal proposal will be shared and voted during next semiannual meeting.

- Most felt that no much change is needed at present time in the Group governance and asks Dr. Gronchi to continue leading the group for the time being.
- Rotating Chair of the Group every year is not felt as a need, and may actually affect continuity in leading the Group.
- Most agreed that the structure of working Commitee and a small Council may be set up in order to keep improving, but not in a rigid formal structure. This may allow to have different leads for the Group activities. Young members should be encouraged to get involved.

ACTION: a call to volunteer in Group leading will be circulated, concerning different activities .

The Meeting is adjourned to next Semiannual Meeting that will be held before SSO in San Diego, CA on Wednesday March, 27th 2019.