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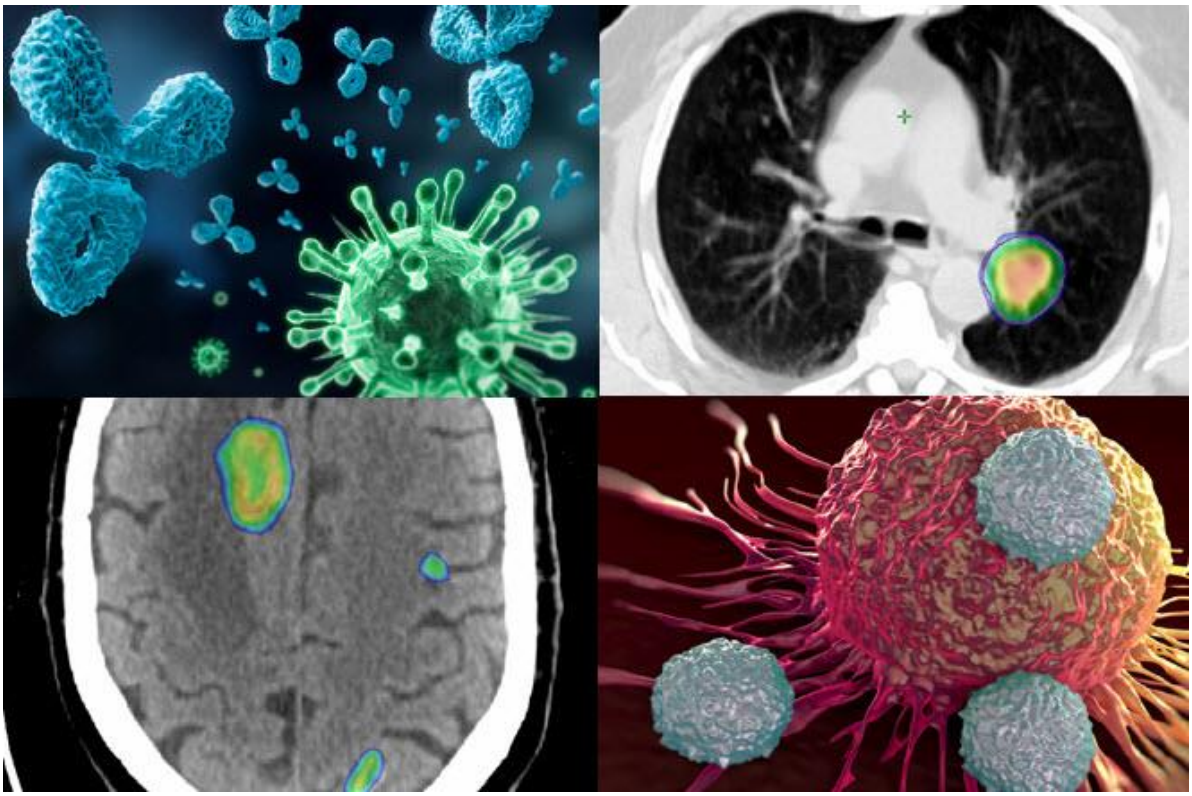

TOXICITY AND EFFICACY OF COMBINED STEREOTACTIC RADIOTHERAPY AND SYSTEMIC TARGETED OR IMMUNE THERAPY

-*TOaSTT*-

A multicentre initiative on behalf of
the DEGRO Working Group Stereotactic Radiotherapy
hosted by the Department of Radiation Oncology – USZ

Dear colleagues,

As we presented on this year's SASRO and DEGRO meeting, we have established a multi-institutional database to evaluate potential risks and outcome of stereotactic radiotherapy combined with targeted therapy and immunotherapy in metastatic cancer patients. The project will collect retrospective patient data and simultaneously start a separate prospective registry trial. This is a project of the DEGRO Working Group Stereotactic Radiotherapy and the database will be hosted by the University Hospital Zurich. The study is open to all interested institutions: We kindly ask you to participate in this initiative.

What is the rationale for this project?

Stereotactic radiotherapy (SRT) - cranial or extra-cranial - has been broadly adopted in our radiation oncology community and is increasingly used in the metastatic setting. In addition, the management of patients with locally recurrent or metastatic cancer has changed fundamentally due to biomarker-based targeted therapies (antibodies, small molecules, immunotherapy). The combination of both may improve outcome and lead to a paradigm shift for "palliative" radiotherapy in the situation of oligo-metastasis and oligo-progression. However, very little is known about this combined modality treatment; especially regarding the risk of toxicity.

What is the background and goal of this project?

According to a recently conducted survey among 27 German speaking centers, the combination of targeted therapy with SRT has already become a routine practice in many of our institutions. Evidence regarding safety and efficacy is therefore urgently needed, but hard to obtain: Prospective safety evaluation in the form of traditional interventional clinical trials would be extremely difficult for all possible permutations of treatment options and radiation practices.

We therefore propose an international, multi-institutional database to evaluate the risk of severe acute and late toxicity of combined targeted therapy or immunotherapy and SRT. The study consists of two components, which will be independent from each other: a retrospective study and a prospective registry study. Primary endpoint is acute and late toxicity; secondary endpoints are OS, PFS, local tumor control and patterns of disease progression.

What are eligibility criteria for inclusion into this study?

Eligibility criteria for inclusion into this study will be treatment of any cranial or extra-cranial metastatic tumor/recurrence or primary tumor (e.g. HCC) with SRT AND simultaneous treatment with any type of targeted therapy (antibodies, small molecules, immunotherapy). Patients should be ≥18 years old. Concomitant treatment is defined as SRT within + / - 30 days prior and after the application of the systemic treatment. SRT will be defined as delivery of minimum 50Gy (2Gy-equavalent dose; alpha/beta of 10Gy) in maximum 10 treatment fractions. The definition of SRT independent from the radiotherapy delivery technology: linac-based SRT, robotic SRT or Gammaknife.

What is the workload associated with this study?

Each center will need local ethics approval: we will assist by providing background information and all usual documents required for submission to the ethics committee. Centers can participate in the retrospective and prospective study independently. In the retrospective study, data entry will require approximately 30 min for 1 patient. The prospective registry study will collect data 3, 12 and 24 months after SRT. All data will be entered into an online database using the RedCap©-Software.

Currently, we are not able to provide patients fees; this may change if grant applications are successful.

What is the timeline of this project?

Both the retrospective and prospective studies will be launched in January 2017. Detailed study information will be provided via email and has been presented at the Working Group Meeting in Zurich December 10th. The collection of retrospective data is planned to be completed in summer 2017.

What can you expect from your participation?

According to the previous and successful practice of the working group, all participating centres will be co-authors on all publications. Results will be presented and discussed at the twice-annual working group meeting to ensure rapid distribution of new knowledge.

In previous projects of this working group with a similar project structure, data of overall >1500 patients were collected. This resulted in eight publications in peer-reviewed journals, and more are to come.

We would like to ask you to confirm your interest in this project by responding to SBRT.radioonkologie@usz.ch **and include the name of the contact person for your institution. Important information for our Swiss colleagues: As we will place the Swiss ethics proposal here in Zurich please inform us promptly about whom will be responsible for conduct within your institution.**

In case of any questions, contact us at any time.

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