

CASE REPORT:

Multimodal oncologic therapy of the malign melanoma

New targeted therapies play an increasingly significant role in the therapy of cancer patients. In combination with advances in medical imaging, opportunities and challenges result for the interdisciplinary therapy setting. Prof. Dr. Heinz-Peter Schlemmer, head of the radiology department of the German Cancer Research Center, summarizes the challenges: "Multi-disciplinary therapy approaches combined with multimodal and multi-parametric imaging procedures and their frequent application during therapy lead to new complexities in the radiological evaluation of oncologic patients."

A patient example for this is a 48-year-old female patient with malign melanoma of the left thigh. An initial staging via CT raises suspicion of malign lymph nodes inguinal left and paraaortic/iliacal left. The therapy is structured into several periods over a time span of about a year:

After a lymph node dissection inguinal left and paraaortic/iliacal left and subsequent targeted therapy with the monoclonal antibody Ipilimumab, new skin metastases occur on the left thigh. These metastases are excised.

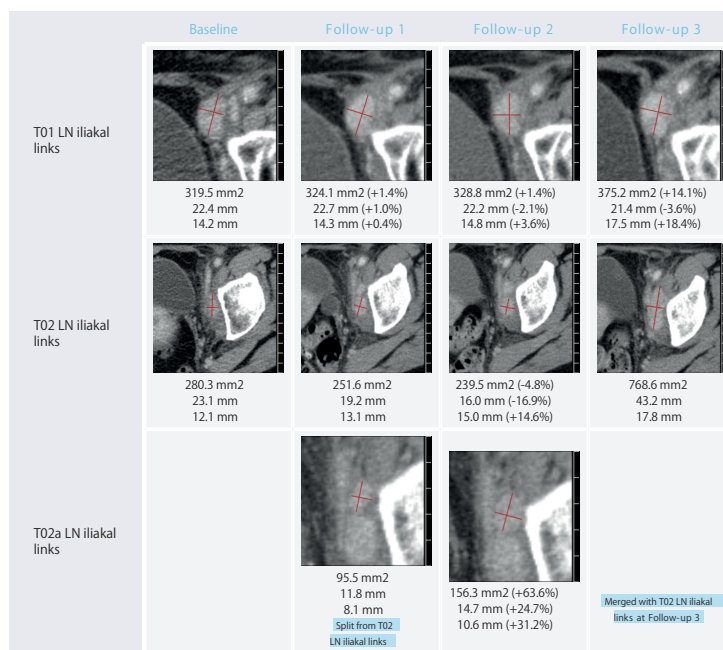


Figure 1:

Prominent iliac lymph nodes left in the course of therapy

After 3 months of therapy, the imaging shows some lesions as progressive, others as stable or regressive. Overall, the radiological diagnosis still results in "Stable Disease". Based on this categorization and on a slight progression of main metastases, the patient decides on participating in a clinical study for the PDE inhibitor Tadalafil. After two months of therapy a progression in size of the skin tumor on the thigh is identified. An MRT of the head shows several small new brain metastases. The therapy scheme is changed to the BRAF inhibitor Vemurafenib. In the following examinations, the patient shows good therapy response.

The evaluation of the therapy response to the antibody therapy with Ipilimumab was done using the Immune Related Response Criteria (irRC). Here, new metastases do not automatically lead to "Progressive Disease". Despite new lesions at the follow-up 1, the time point response is "Stable Disease" because the overall sum (tumor burden) has grown less than 25% compared to Nadir (baseline in this case) (see table 1). In this diagnosis, the target lesion T02 also is splitted into two clearly separated lymph nodes which merged together again at the follow-up 3 (see figure 1). This special situation of adjacent, similarly sized and contrarily developing lesions complicates the consistent evaluation and bears the danger of a false assignment or evaluation of the reference lesion. Prof. Dr. Schlemmer is well aware of the importance of a consistent evaluation: "The consistent evaluation and documentation of the individual therapy periods is indispensable as radiological contribution for the interdisciplinary therapy setting."

In the year 2009, radiologists and IT specialists from the German Cancer Research Center have begun to work on a software solution "mint Lesion" as a "workflow tool" for the daily needs of managing these and similar patient cases. Standardized documentation of the oncologic diagnosis by mint Lesion allows for an overview over various therapy periods: mint Lesion refers to an arbitrary baseline examination and highlights possible turning points.

	Baseline	Follow-up 1	Follow-up 2	Follow-up 3
Target sum	701.1 mm ²	775.3 mm ² (+10.6%)	807.2 mm ² (+4.1%)	1,233.1 mm ² (+52.8%)
New lesion sum	--	97.1 mm ²	136.5 mm ² (+40.6%)	209.1 mm ² (+53.2%)
Tumor burden	701.1 mm ²	872.4 mm ² (+24.4%)	943.7 mm ² (+8.2%)	1,442.2 mm ² (+52.8%)
Target response	Undefined	Stable Disease	Progressive Disease	Progressive Disease
Non-target response	Undefined	Stable Disease	Stable Disease	Stable Disease
New (non-measurable) lesions	No	No	No	No
Timepoint response	Undefined	Stable Disease (ir)	Progressive Disease (ir)	Progressive Disease (ir)

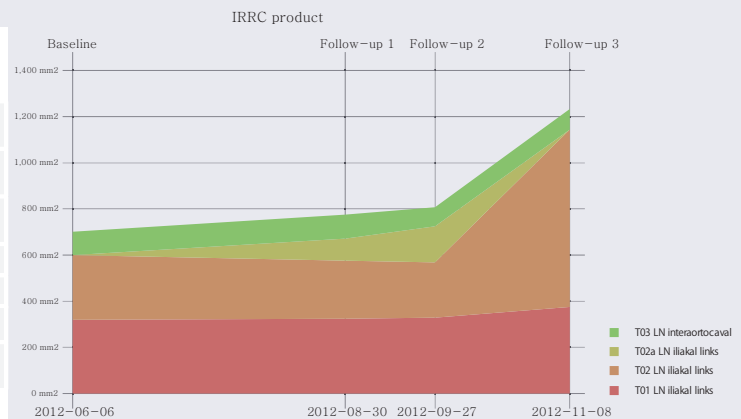


Table 1: Evaluation of the response behavior based on the Immune Related Response Criteria (irRC), Wolchok et al, Clin Cancer Res 2009;15(23)

Diagram 1: Contribution of each of the target lesions to the overall tumor burden (irRC product) throughout the course of therapy

If the therapy scheme or the applied radiological evaluation criteria changes, already evaluated lesions can be reused. The inconsistent response of lesions, like in the above example, is pointed out transparently. Splitting or merging lesions can be depicted explicitly too – a uniformly-scaled depiction of the lesions in the course of therapy ensures correct assignment. Different readers can easily reproduce the therapy progression and contribute to a consistent evaluation, confirms Prof. Dr. Schlemmer: "A neat solution – solidly based on many years of clinical experience and implemented in detail to meet the day-to-day demands professionally."