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"Fraction", "Cycle" or a new terminology? What would be most appropriate for Molecular Targeted Radiotherapy with Unsealed Sources?

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"Fraction", "Cycle" or a new terminology? What would be most appropriate for Molecular Targeted Radiotherapy with Unsealed Sources?

Targeted radionuclide therapy with unsealed sources constitutes a unique form of therapy that encompasses the characteristics of both radiotherapy and systemic chemotherapy to a varying extent. Its administration, delivery and localization can be viewed akin to that of a systemic pharmaceutical while the resultant therapeutic effect at the cellular target is primarily by the radiation dose delivered by the radiopharmaceutical. The therapeutic agent is localized at the target by a particular metabolic pathway or through cell surface receptors, enzymes or peptides that have been probed by prior diagnostic imaging, forming the basis of "theranostics", a popular term of recent years in the domain of unsealed molecular based radionuclide therapy.

The dose schedule in chemotherapy is typically described by 'cycle' (where a course consists of multiple cycles of chemotherapy with an interim rest period between two cycles), while the individual radiotherapy doses are denoted as 'fractions'. For the unsealed radiopharmaceutical therapy, to emphasize the final therapeutic effect at the target (which is primarily by radiation induced DNA damage), each individual dose has been denoted traditionally by the term "fraction" in the initial years. In the recent years, however, "cycle" has been more frequently used (including in guidelines) particularly for treatment with intravenous radiopharmaceuticals [such as peptide receptor radionuclide therapy (PRRT) with 177Lu/90YDOTATATE] that is usually scheduled at a regular interval multiple times, each termed as "one cycle" [1]. One can partly conceive this trend shift due to the apparent similarity of the newer intravenous therapies with systemic chemotherapies, including the issues encountered and their management. Truly, the current therapies such as PRRT, to a substantial extent has similarity with chemotherapy schedules (including complete and efficient management of associated complications such as emesis and others both during therapy or during the post-treatment period that demand a very sound medical knowledge from the

attending Nuclear Medicine physicians). In day-to-day practice, however, both "fraction" and "cycle" are frequently used interchangeably.

Another perspective is the concept of dose fractionation. Dose fractionation schedules in systemic radionuclide therapy continues to be in the process of evolution and compared to that of external radiotherapy, relatively less well-defined at present; amongst many factors, this is likely to be governed by the effect achieved, the intent of therapy (neoadjuvant versus palliative) and the biology of the tumor in question [2]. Interestingly, when the dose is fractionated based on these characteristics, the fractionated doses are at times referred to as cycles administered to the patient.

With the progression of theranostics and radionuclide therapies and introduction of several novel unsealed systemic therapeutic agents (including the introduction of alpha emitting radiopharmaceutical) into the clinical domain, it can be foreseen that the future potential of this form of therapy is likely to expand rapidly in coming years. Hence, understanding the complexities of dosimetry related radiobiology and appropriating the associated terminologies pertaining to the dose schedule is a need of the hour and ought to be considered by the Nuclear Medicine fraternity.

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