LUTETIUM-177 – BROAD PRODUCTION CAPABILITIES ARE EXPECTED TO STIMULATE CLINICAL APPLICATIONS OF THIS IMPORTANT THERAPEUTIC RADIOISOTOPE

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Lutetium-177 (Lu-177) is of broad interest for therapeutic applications where the deposition of localized radiation can benefit from the limited soft tissue penetration of the 0.497 MeV beta particle (max. = 2.76 mm). Examples of Lu-177 therapeutic strategies include treatment of small SS2/SS5-expressing tumors with targeted peptides and radiosynovectomy. Emission of a 208 keV gamma photon (11 %) allows imaging for evaluation of localization and biokinetics, and for targeting applications, correlation of uptake with therapeutic response. A broad spectrum of research reactors with even modest thermal neutron flux (e.g. > 1 x 10^{14}) can produce carrier-added Lu-177 with sufficient specific activity (SA) > 10 Ci/mg Lu by the "direct" approach by irradiation of Lu-176. For low SA applications, thermal flux of > 10^{13} in low-medium flux reactors provides sufficient SA (> 0.5 mCi Lu-177/mg) for preparation of Lu-EDTMP for synovectomy. Although relative Lu-177m/Lu-177 activity levels from "direct" production can be very low (> 10^{-5}), the Lu-177m impurity levels can present an issue with radioactive waste storage requirements at some institutions. The alternative "indirect" approach using decay of reactor produced ytterbium-177 available from by neutron irradiation of enriched Yb-176 targets provides no-carrier-added (nca) Lu-177 (theoretical SA = 109 Ci/mg Lu). Purification of the microscopic levels of nca Lu-177 from macroscopic Yb levels at the high multi Curie production level is a more challenging approach, since production yields are relatively low even at high thermal flux (e.g. < 300 mCi Lu-177/mg Yb at > 2 x 10^{15} neutrons/cm2/sec). In addition, high mass Lu/Yb separation is especially time consuming, can generate significant waste, and the relatively expensive Yb-176 target material (> 97%, ~ $ 20/mg) must be recovered, re-purified and used for subsequent target preparation. However, a number of effective methods for the Lu/Yb separation and Yb recovery have been reported, and even though the effort and expense increase exponentially as higher levels of nca Lu-177 are required, with more experience, these methods would be expected to be optimized and automated. Effective clinical results of targeted therapy exemplified with Lu-177-DOTAT-TOC and other peptides have been widely reported for neuroendocrine tumors. For this application, SA of probably > 10 Ci/mg is required. For arthritis therapy with Lu-177-EDTMP, much lower SA is sufficient (~ 0.5 Ci Lu-177/mg). Although not yet realized, the unique opportunity to produce high activity levels/high SA Lu-177 essentially anywhere in the world would be expected to catalyze broader clinical use of Lu-177. In fact, this is a unique situation where production capabilities for both HSA and LSA Lu-177 far exceed current demand. The goals of this presentation are to discuss the issues associated with the routine production and processing of high activity levels of lutetium-177 and current and expected clinical applications.

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