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EDITORIAL

All of the Above (With Caveats for Each)

The choice of radioimmunoconjugate in radioimmunotherapy (RIT) has been the subject of study and speculation for years. Two different and yet similar approaches to RIT are discussed in this issue of the *JNM* (*1,2*). Juweid et al. (*1*) describe their results with ^{188}Re-labeled anti-CEA antibody in patients with GI cancers and speculate on the utility of fractionated RIT (*3*) using short-lived radionuclides. Zhang et al. (*2*) used a two-step targeting technique to increase the therapeutic ratio of ^{90}Y and alleviate marrow toxicity.

Apart from the striking similarity in the beta-minus emissions of the two radionuclides (*4*), the studies underscore the need to improve the current dismal response rates seen with radioimmunotherapy in solid tumors. And they raise the issue of what radioimmunoconjugate would be ideal for successful RIT in solid tumors.

The sustained clinical responses seen in patients with B-cell lymphoma treated with radioimmunotherapy (*5,6*) have encouraged researchers to search for ways to obtain comparable successes in solid tumors. However, current trials have achieved modest results (*1,2,7–11*), despite dose-intensification schema that include bone marrow transplants (*12*). There is, thus, a need to define those characteristics that would make a radioimmunoconjugate likely to achieve major responses in solid tumors.

Initial RIT trials have been, and will be, carried out in patients with bulky disease who have failed conventional chemotherapy—a group least likely to respond to any therapy. Logically, bulkier disease would necessitate the use of long-lived nuclides with energetic beta-minus emissions capable of traversing the tumor. These nuclides would ideally be conjugated with intact immunoglobulins, to allow persistence of radioantibody in circulation with consequent accessibility to tumor.

Riethmuller et al. (*13*) found that patients with surgically treated Duke's C colon carcinoma who had received unlabeled MAb 17-1A, that reacts against an epithelial surface antigen (*14*), had longer disease-free and overall survivals than their randomized controls. Similar results, albeit in a nonrandomized trial, were reported by Epenetos' group using ^{90}Y-labeled anti-mucin MAb (*15*).

Yttrium-90, with its pure beta-minus emission, has the advantage that it can be administered in an outpatient setting, and its companion disadvantage that dosimetric measures cannot be used in treatment calculations. While its energetic beta-minus may make it useful for bulky disease, it may render it less effective for minimal disease, where ^{131}I may well prove more useful, as may less energetic nuclides such as ^{177}Lu. Moreover, current changes in NRC regulations in the U.S. may make it possible for larger amounts of ^{131}I-labeled MAbs to be administered to outpatients (*16*). Many other nuclides already may be administered to outpatients, including ^{186}Re (*17*), ^{177}Lu and the ^{188}Re used by Juweid et al. (*1*). Finally, the use of positron-emitting nuclides such as ^{86}Y (*18*) and ^{64}Cu (*19*) will permit understanding of the biokinetics of ^{90}Y, ^{67}Cu and other pure beta-emitters.

The increasing use of radioimmunoconjugates of all types in solid tumor therapy can only augur well for the future. Tailored therapy, stated so clearly by Humm and Cobb (*20*) and O'Donoghue et al. (*21*), entails the selection of a radionuclide with appropriate decay and emission characteristics, conjugated to a macromolecule of appropriate immunobiologic characteristics. It is possible to envisage the development of multi-step techniques using radionuclides of ever shorter path length attached to nonimmunogenic antigen-binding proteins of faster biologic clearance to treat ever smaller disease burdens.

Is differential tumor uptake of radioimmunoconjugate, however, sufficient for effective treatment, regardless of the nature of the radioimmunoconjugate? Another multi-step approach (*2*) therefore seeks to increase the differential uptake of radioactivity in tumor. Antibodies of dual specificities, with one arm reacting to a tumor associated antigen and the other recognizing a ligand, are first injected. When the antibody has cleared from the circulation, ^{90}Y-labeled ligand is injected, with the intention of increasing relative tumor uptake and thus minimizing toxicity. This promising approach is already in clinical trials. It is becoming apparent that many issues, including immunogenicity and nonspecific accumulation in organs such as the liver, will need to be addressed (*22–24*).

The development of targeted radiotherapy has been fraught with uncertainties, offset significantly by developments in protein chemistry, bioengineering and nuclear chemistry. With the development of nonimmunogenic molecules of varying size and biologic function (*25–32*), we are now on the threshold of becoming able to tailor targeted radiotherapy. Let us use all the weapons in our armamentarium, and use each wisely.

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Diagnostic Accuracy of Technetium-99m-Pertechnetate Scintigraphy with Lemon Juice Stimulation to Evaluate Warthin's Tumor

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This study investigated the diagnostic accuracy of ^{99m}Tc-pertechnetate scintigraphy with lemon juice stimulation for evaluating parotid gland Warthin's tumor. **Methods:** Technetium-99m-pertechnetate scintigraphy with intraoral lemon juice stimulation was used to evaluate a total of 68 parotid gland lesions clinically suspected of being Warthin's tumor in 62 patients. Twenty-three of the 68 lesions were subsequently histologically confirmed to be Warthin's tumor, whereas the remaining 45 lesions were histologically diagnosed as being other lesions. **Results:** Technetium-99m-pertechnetate scintigraphy with lemon juice stimulation correctly diagnosed 18 of 23 Warthin's tumors as being Warthin's tumor but was unable to diagnose the other five Warthin's tumors. Further, scintigraphy correctly diagnosed 41 of 45 non-Warthin's tumors as being non-Warthin's tumor but misdiagnosed other four non-Warthin's tumors as Warthin's tumor. Thus, the sensitivity of scintigraphy for diagnosing Warthin's tumor was found to be 78%, its specificity 91% and its accuracy 87%. On the basis of prestimulation images alone, however, the sensitivity was estimated to be 65%, its specificity 93% and its accuracy 84%. **Conclusion:** For evaluating Warthin's tumor, the sensitivity of ^{99m}Tc-pertechnetate scintigraphy was relatively low, although the specificity was sufficiently high. Lemon juice stimulation improved the sensitivity markedly but decreased the specificity slightly. Thus, ^{99m}Tc-pertechnetate scintigraphy with lemon juice stimulation should be carefully performed for diagnosis of Warthin's tumor.

Key Words: Warthin's tumor; parotid gland; neoplasms; technetium-99m-pertechnetate; lemon juice stimulation

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