Phase I/II Trial of ^{111}In -Labeled Anti-CEA Monoclonal Antibody (^{111}In -ZCE-025) in Diagnosis of Colorectal Cancer

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A phase I/II study of imaging with radiolabeled anti-CEA monoclonal antibody, ^{111}In -ZCE-025, was carried out in patients with colorectal cancers as a joint research project at 5 hospitals in Japan. There were 24 patients, 22 of which were judged to be evaluable. Nineteen had primary lesions with or without metastatic lesions, two had local recurrences, and one had only metastatic lesions. On the patient basis, 21 of the 22 (95.5%) were judged to be positive. Of the 40 known lesions, planar imaging detected 24 (60.0%), whereas combined imaging (planar and single photon emission computed tomography, SPECT) detected 29 (72.5%). Surgery disclosed another 22 new lesions, two (9.1%) of which had been detected by the planar and four (18.2%) by the combined imagings. As for the newly visualized sites, on the other hand, planar imaging depicted 10, two of which were true positives (20.0%), whereas combined imaging depicted 20 and four of which were true positives (20.0%). These low positive predictive values for newly visualized sites were due to many false positive lymph nodes.

In conclusion, this method will be useful for preoperative screening and diagnosis of local recurrence of colorectal cancers. But the formation of HAMA should be taken into consideration when this method is repeatedly used. At present, for metastatic foci in lymph nodes, this method possesses only a complementary role.

Key Words: monoclonal antibody (ZCE-025), radioimmunoscintigraphy,
colorectal cancer, human anti-mouse antibody

1. Introduction

Since Köhler and Milstein¹⁾ established the cell-fusion technique for the production of specific antibodies against certain diseases, monoclonal antibodies (MoAbs) have attracted attention for their potential application in drug delivery systems. In the field of nuclear medicine, radiolabeled monoclonal antibodies, called radioimmunoconjugates, are now under intensive investigation on a world-wide scale not only for imaging but also for the treatment of cancer patients. This paper reports the results of a phase I/II study of a radiolabeled anti-CEA monoclonal antibody, ¹¹¹In-ZCE-025, in the diagnosis of colorectal cancer. This study was carried out as a joint research project at 5 hospitals in Japan.

2. Materials and Methods

2.1 Patients

The eligible subjects for this study were patients with colorectal carcinoma scheduled for surgery within 20 days after antibody administration. There were 24 patients, and 9 of them had primary lesions only, 10 had both primary and metastatic lesions, and the remaining 5 were postsurgical and were known to have metastases or suspected to have recurrence. Two patients were eventually excluded from the imaging evaluation, one because of postsurgical stenosis and the other due to a different type of malignant disease (carcinoma of the uterus). Prior to MoAb infusion, all patients were examined clinically and assessed for their hematological and biochemical profiles as well as urinalyses. A skin test was performed prior to MoAb infusion anticipating "pre-existing" human anti-mouse antibody (HAMA). Informed consent was obtained from all the patients, and the procedure was approved by each Institutional Review Board.

2.2 Antibody and radiolabeling

ZCE-025, an anti-CEA MoAb, was provided by Hybritech Inc. (California, USA) through Teijin Ltd. (Osaka, Japan). ZCE-025 is a murine antibody of immunoglobulin G1(IgG1), and is the same antibody that was designated as MAB-35 by Mach et al.²⁾ Two different forms of antibodies were supplied in a kit form; one as diethylenetriaminepentaacetic acid (DTPA) conjugated ZCE-025 (thereafter DTPA conjugated ZCE-025) for labeling and

the other as chemically unmodified ZCE-025.

Labeling was performed at each hospital prior to administration to the patients following Hybritech's instructions. Namely, 74 to 111 MBq (2 to 3 mCi) of ¹¹¹InCl₃ (Nihon Mediphysics Co., Ltd.; Takarazuka, Japan) was mixed with citrate buffer solution (1 ml). This was added to the DTPA conjugated ZCE-025 solution (antibody 2 mg, 2 ml) in a reaction vial. After 30 minutes' incubation, a neutralizing buffer solution (4 ml) containing excess DTPA was added to the reaction solution to scavenge any unincorporated ¹¹¹In. The labeling efficiency was determined by thin layer chromatography (TLC). The solution was used only when the labeling efficiency was 80% or more.

2.3 Antibody administration and imaging

Prior to the administration, the solution containing ¹¹¹In-labeled ZCE-025 was mixed with approximately 100 ml of physiological saline which had already been mixed with unmodified ZCE-025 solution (antibody 40 mg, 40 ml). The final solution was administered by i.v. drip infusion over a period of about one hour. The vital signs were monitored during the infusion as well as for about one hour post-infusion. Hematological and biochemical assessments and urinalysis were performed after about 3 days to monitor the toxicity. This part of the protocol was set employing the data provided by Hybritech Inc.

Images of regions of interest and/or whole-body images were obtained 3 days after the administration and, if possible, at other time points. Single photon emission computed tomography (SPECT) was also performed as often as possible.

2.4 Pharmacokinetic study

Heparinized blood samples were collected at various intervals between the completion of the infusion and 130 h (62–192 h) after the infusion on average. A small aliquot of injected solution was retained to serve as a standard and isotope decay. Urine samples were also collected for 3 days for excretion studies.

2.5 Human anti-mouse antibody (HAMA)

Serum was collected at various intervals and was stored by freezing at –20 °C. HAMA titers were determined using an enzyme-linked

immunosorbent assay (ELISA). Polyvinyl chloride 96-well plates (Falcon flexible plate # 3912; Becton Dickinson Co. Ltd.; Franklin Lakes, NJ) were coated with $1\text{ }\mu\text{g}$ per well of ZCE-025, and then the plates were blocked with phosphate buffered saline (PBS) containing 1% bovine serum albumin. Serum samples ($100\text{ }\mu\text{l}$) at various dilutions were added and incubated for 1 h. The plates were washed three times and $100\text{ }\mu\text{l}$ of a 1:2 000 dilution of peroxidase-conjugated goat anti-mouse IgG antibody (Tago Inc.; Burlingame, CA) was added to each well and held for 1 h at room temperature. The plates were washed three times, and $200\text{ }\mu\text{l}$ of *p*-nitrophenyl phosphate solution (0.6 mg/ml) was added and held for 30 min. The optical density was determined at 405 nm using a micro-ELISA reader (Titertek multiscan; Flow Lab. Ltd.; Irvine, Scotland). The titer was defined as the dilution required to obtain a cutoff absorbance value.

2.6 Immunohistochemical staining

Immunohistochemical staining was performed by the avidin-biotin-peroxidase complex method. In brief, formalin-fixed, paraffin-embedded surgical specimens were sectioned, dewaxed and rehydrated. Endogenous peroxidase was blocked with 0.3% hydrogen peroxide in methanol. Primary antibody ZCE-025 was applied at a 1:80 dilution for 1 h at room temperature. After washing the sections with PBS, the secondary antibody, *i.e.*, biotinylated horse anti-mouse antibody (Vector Laboratories Inc., Burlingame, CA), was applied at a 1:250 dilution for 30 min. After washing with PBS, avidin-biotin-peroxidase complex (Vector Laboratories Inc.) was applied at a 1:80 dilution. The reaction product was developed in diaminobenzidine and counterstained with Mayer's hematoxylin.

3. Results

3.1 Labeling efficiency

The average labeling efficiency for all 24 patients ($\bar{x} \pm \text{SD}$) was $88.5 \pm 5.3\%$, whereas for 17 patients subjected to urinary excretion studies it was $88.0 \pm 5.3\%$. Some of the preparations were assessed using TLC as well as size-exclusion high performance liquid chromatography (HPLC) and paper chromatography. The radioactivity not associated with the antibody was neither in the ionic form nor colloid but was bound to the DTPA.

The labeled antibody was found to retain sufficiently the immunoreactivity assessed by a live cell binding assay.

3.2 Pharmacokinetics

The radioactivity in blood samples was determined for 21 patients. The time dependency of the radioactivity was analyzed by the two compartment model for each patient. The average biological half-time of the radioactive materials for the alpha and beta phases were 14.2 h ($0.93 - 40.5\text{ h}$) and 88.6 h ($32.8 - 210\text{ h}$), respectively.

Urinary excretion was determined in 17 patients. The average excretion of radioactive materials was 14.6% ID ($9.9 - 25.4\%$ ID) for 0 - 24 h, 1.7% ID ($0.87 - 2.9\%$ ID) for 24 - 48 h and 1.9% ID ($1.05 - 3.8\%$ ID) for 48 - 72 h. From the results of labeling efficiency, the average radioactivity unincorporated to antibodies for these 17 patients was 12.0% ID, which was considered to be excreted mainly within the first 24 h after infusion.

3.3 Imaging results

The patients' characteristics and the results for all 24 patients are summarized in Table 1. Twenty-two patients underwent surgery after imaging examinations. The scintigraphic findings were evaluated by surgery in these patients. One patient (No. 2 in Table 1) did not undergo surgery because the suspected lesion was finally diagnosed as radiation proctocolitis which occurred after radiotherapy for carcinoma of uterus. Another patient (No. 4 in Table 1) did not undergo surgery because invasion of a rectal carcinoma into the sacroiliac joint was confirmed by X-ray CT and magnetic resonance imaging.

In this study, each lesion was, in principle, counted as one. However, because of the limitations of image resolution, complete separation of each lesion was impossible in some cases, especially for lymph nodes and multiple liver metastases. In such cases, these lesions were counted as one on the basis of the anatomical region.

The sensitivity on patient basis was 95.5% (21/22). The scintigraphic results on the basis of the number of lesions are summarized in Table 2. Of 40 known lesions, 24 (60%) were detected by planar imaging (PI). When SPECT imaging was performed together with PI (combined imaging), 29 of 40 lesions (72.5%) were judged positive.

Table 1 Summary of diagnoses and results

Case No.	Sex/Age	Diagnosis	No. of known lesions	Immunoscintigraphy						
				Known lesions		New foci			Confirmed lesions	
				TP	FN	TP	NC	FP	TP	FN
1	F/57	Colon ca., recurrent	0	0	0	0	0	0	0	3
2*	F/59	Uterus ca., recurrent	0	0	0	0	0	0	0	0
3	M/73	Rectal ca.	3	1	2	1	0	0	2	2
4	F/36	Rectal ca., local rec.	1	1	0	0	0	0	1	0
5	M/57	A. colon ca.	1	1	0	0	0	1	1	0
6	M/50	Rectal ca.	1	1	0	0	0	0	1	0
7	M/64	A. colon ca.	3	1	2	1	0	0	2	3
8	F/75	Rectal ca.	1	1	0	0	0	2	1	0
9	M/76	Rectal ca.	2	2	0	1	0	6	3	1
10	M/45	T. colon ca.	1	1	0	0	0	0	1	0
11	F/64	A. colon ca.	1	1	0	0	0	0	1	0
12*	M/46	Postoperative stenosis	0	0	0	0	0	0	0	0
13	F/68	S. colon ca.	2	2	0	0	0	1	2	0
14	M/70	T. colon ca.	2	1	1	0	0	0	1	1
15	M/44	Rectal ca.	1	1	0	0	0	0	1	1
16	M/51	S. colon ca.	9	4	5	0	0	1	4	6
17	M/66	S. colon ca.	3	3	0	0	0	5	3	5
18	M/70	Rectal ca.	3	2	1	0	0	0	2	2
19	F/55	Rectal ca.	1	1	0	0	0	0	1	0
20	F/55	Rectal ca.	1	1	0	0	0	0	1	0
21	M/61	Rectal ca., local rec.	1	1	0	0	0	0	2	0
22	M/77	S. colon ca.	1	1	0	0	0	0	1	0
23	M/56	S. colon ca.	1	1	0	0	0	0	1	5
24	F/55	S. colon ca.	1	1	0	0	0	0	1	0
Total			40	29	11	4	0	16	33	29

* Excluded from analysis of efficacy.

TP: True positive, FN: False negative

FP: False positive, NC: Not confirmed

Table 2 Summary of imaging results

Type of imaging	Known lesions			New foci imaged		New lesions confirmed at surgery	
	No. of lesions	No. of lesions detected	No. of foci	True positive	False positive	No. of lesions	No. of lesions detected
Planar	40	24(60.0%)	10	2(20.0%)	8(80.0%)	22	2(9.1%)
Combined imaging		29(72.5%)	20	4(20.0%)	16(80.0%)		4(18.1%)

Ten new sites were depicted by PI, 2 of which were true positive, whereas combined imaging depicted 20 new sites, 4 of which were true positive.

On the other hand, surgery disclosed 22 new lesions, and PI and combined imaging detected 2 lesions (9.1%) and 4 lesions (18.2%), respectively. The overall sensitivity was calculated as 41.9% [26/(40+22)] for PI and 53.2% [33/

(40+22)] for combined imaging.

Subsequently, the positive predictive values [TP/(TP+FP)] for PI and combined imaging were calculated as 76.5% [26/(26+8)] and 67.3% [33/(33+16)], respectively. When only newly visualized sites were considered, however, the positive predictive value was 20.0% for both modalities, *i.e.*, 2/10 for PI and 4/20 for combined imaging. Now, the accuracy

Table 3 Detection rate by tumor size

Tumor size (mm)	Detection rate (%)					
	Primary, local recurrence		Metastatic		Total	
	Planar	Combined imaging	Planar	Combined imaging	Planar	Combined imaging
<10	—	—	0 (0/10)	0 (0/10)	0 (0/10)	0 (0/10)
<20	—	—	0 (0/9)	22.2(2/9)	0 (0/9)	22.2(2/9)
<30	—	—	14.3(1/7)	57.1(4/7)	14.3(1/7)	57.1(4/7)
<40	100 (3/3)	100 (3/3)	20.0(1/5)	40.0(2/5)	50.0(4/8)	62.5(5/8)
<50	100 (3/3)	100 (3/3)	25.0(1/4)	25.0(1/4)	57.1(4/7)	57.1(4/7)
≥50	100 (15/15)	100 (15/15)	50.0(1/2)	100 (2/2)	94.1(16/17)	100 (17/17)
Unknown	—	—	25.0(1/4)	25.0(1/4)	25.0(1/4)	25.0(1/4)
Total	100 (21/21)	100 (21/21)	12.2(5/41)	29.3(12/41)	41.9(26/62)	53.2(33/62)

Table 4 Detection rate by site of lesion

Site of lesion	Detection rate (%)	
	Planar	Combined imaging
Primary lesion	100 (19/19)	100 (19/19)
Local recurrent lesion	100 (2/2)	100 (2/2)
Liver	8.7(2/23)	30.4(7/23)
Lymph node	11.8(2/17)	23.5(4/17)
Peritoneum	100 (1/1)	100 (1/1)
Total	41.9(26/62)	53.2(33/62)

$[(\text{TP}+\text{TN})/(\text{TP}+\text{TN}+\text{FP}+\text{FN})]$ can be calculated as 37.1% $[26/(26+8+36)]$ for PI and 42.3% $[33/(33+16+29)]$ for combined imaging, where TN was taken as zero.

The detectability, assessed by the size and location of the lesions, is summarized in Table 3 and Table 4. All primary lesions and recurrent lesions were depicted by both PI and combined imagings. But none of them was less than 20 mm in diameter. On the other hand, the detectability of metastatic lesions was low, *i.e.*, 12.2% by PI and 29.3% by combined imaging. But these values increased slightly when considering only the lesions which were more than 20 mm in diameter; namely, 22.2% by PI and 50.0% by combined imaging.

When lesions were assessed on the basis of their location, lymph node metastases were the most difficult lesions to be detected on the scan together with intrahepatic metastases which were easily obscured by the radioactivity in the adjacent normal liver tissue. On the other hand, primary lesions as well as recurrent lesions seemed to be good targets

Table 5 Detection rate of patients by serum CEA level

CEA level (ng/ml)	Rate of patients with lesions detected (%)
≤ 2.5	100 (10/10)
≤10	85.7(6/7)
≤20	100 (2/2)
>20	100 (3/3)
Total	95.5(21/22)

Normal range of CEA: ≤2.5 ng/ml

for imaging.

Table 5 shows the correlation between the serum CEA level and the results of imaging. The detectability was not affected by the serum CEA level. The normal CEA level in this study was 2.5 ng/ml or less.

3.4 Representative cases

Figure 1 indicates the day-by-day whole-body distribution patterns of ^{111}In -ZCE-025 in a case of carcinoma of the rectum (Case No. 8 in Table 1). Predominant accumulation of the tracer in the liver and long-lasting blood pool images are noted, as well as a definite visualization of the primary lesion.

Figure 2 is a case of carcinoma of the sigmoid colon which was well visualized on the scan (Case No. 24 in the Table 1).

Figure 3 is a case of carcinoma of the transverse colon (Case No. 10 in Table 1). Both planar and SPECT images successfully visualized the primary lesion. Some physiological accumulations of the tracer are noted along the transverse colon as well as the vertebrae. Iliac vessels are also seen.

Fig. 1 Day-by-day whole-body images of Case No. 8 in Table 1 (carcinoma of the rectum).

Figure 4 is a case of carcinoma of the sigmoid colon, which was well visualized in the whole-body scan (Case No. 17 in Table 1). Four other accumulations are noted along the midline of the upper abdomen as well as a faint accumulation in the left supraclavicular region. Histological examination revealed all of these accumulations to be free of tumors except for the primary lesion.

3.5 Immunohistochemical staining

Tumor tissue specimens for immunohistochemical staining were taken from 20 lesions in 18 patients and non-tumor specimens were taken from 16 sites in 15 patients, including the patient with stenosis. The results of

Fig. 3 Planar image (a) and SPECT image (b) of Case No. 10 in Table 1 (carcinoma of the transverse colon).

Fig. 2 Photos of barium enema (a) and planar image (b) of Case No. 24 in Table 1 (carcinoma of the sigmoid colon).

Fig. 4 Anterior (left) and posterior (right) planar images of Case No. 17 in Table 1 (carcinoma of the sigmoid colon).

A: Primary lesion (true positive). B, C, D and E: Paraaortic lymph nodes (false positive). F: Left supraclavicular lymph node (false positive).

staining are shown in Table 6. Although one out of 16 specimens from the colon and rectal lesions was not stained positively, all 16 lesions were detected by immunomaging. Three specimens of intrahepatic metastases stained positively, but only one lesion was detected by the imaging. The remaining one specimen, of a local recurrent lesion (pre-sacral), stained positively and it was detected by imaging.

Ten of 14 specimens taken from the normal colon and rectum stained positively. Two specimens from normal livers stained negatively.

3.6 Side effects

The skin test was negative for all patients. Only two patients experienced short-term reactions. One patient complained of urticaria and pruritus, and the other complained of urticaria. In both cases, these side effects

Table 6 Immunohistochemical staining

Tissue	No. of lesions	Positively stained	
Tumor	Colon and rectum	16	15
	Liver	3	3
	Local recurrence	1	1
Non-tumor	Colon and rectum	14	10
	Liver	2	0

Fig. 5 Time course of HAMA titers.

Dotted line shows results of the patient whose pre-infusion serum sample was not measured. The titer was defined as the dilution required to obtain a cutoff absorbance value.

were mild. There were no significant changes in the hematological findings, serum biochemical profiles or urinalyses.

3.7 HAMA formation

To check the HAMA titers, serum samples were drawn before and after the infusion of the antibody in 20 patients and only after the infusion in one patient. The titers were found to be elevated as early as one week post-infusion, showing positive HAMA in all cases by about 6 weeks, lasting for more than 30 weeks (Fig. 5).

4. Discussion

Colorectal cancers have been one of the targets of radioimmunoscintigraphy (RIS) in recent years, and such murine antibodies to CEA as ZCE-025⁽³⁾, B7-25⁽⁵⁾, MAB-35⁽⁵⁾, C46⁽⁶⁻⁸⁾, G15⁽⁹⁾, 11-285-14⁽¹⁰⁾, T84.66⁽¹¹⁾, etc., have been widely tested. These antibodies are used

in the form of either the intact antibody or a fragment. In this field, ^{111}In , ^{131}I , and ^{125}I are frequently used for radiolabeling of the antibodies. However, the labeling technique of $^{99\text{m}}\text{Tc}$ is now being investigated⁽¹²⁾ and clinical trials have been reported by some workers⁽¹³⁾.

In our study, 21 of 22 patients gave positive images. Based on the number of lesions, the overall sensitivities were 41.9% with PI and 53.2% with combined imaging. These rather low sensitivities were attributable to the fact that a number of small lesions, which were newly confirmed by surgery, were included. When only lesions of 20 mm or greater were considered, the sensitivities improved to 64.1% and 76.9%, respectively (Table 3).

Although 19 primary tumors and 2 recurrent tumors were correctly diagnosed, the detection rates of liver metastases and lymph node metastases were not sufficient. The sensitivities of combined imaging for these lesions were 30.4% for liver metastases and 23.5% for lymph node metastases. According to Abdel-Nabi et al.⁽³⁾, 18 of 20 documented tumor sites in 15 patients, excluding those in the liver, were depicted with ^{111}In -ZCE-025. In their series, the amount of antibody used ranged from 2.5 to 80 mg, and the sensitivity for liver metastases was 25% as a whole, showing some improvement by increasing the dose of antibody. Because of a high detection rate of 91.7% (11/12) for lymph node metastases, they stated that this technique might be helpful in preoperative staging of colorectal cancer patients, although only lesions of 1.5 cm or greater were taken into consideration in their study. In comparison with intact MoAbs, the clearance of MoAb fragments from the blood is known to be rapid and, therefore, the usage of MoAb fragments in RIS is expected to reduce the background activity and to improve the detection rates. Using F(ab')_2 of ZCE-025 labeled with ^{111}In , Lamki et al.⁽⁴⁾ reported the overall sensitivity for colorectal cancer as 79.4% (54/68) and the sensitivity for liver metastases as 83.8% (31/37). These were higher than the overall sensitivity of 32.0% (39/122) and the sensitivity for liver metastases of 22.2% (10/45), using the intact IgG antibody⁽⁴⁾. Halpern et al.⁽¹⁴⁾ also reported that the detection rates of CEA-producing tumors were 83% (25/30) with ^{111}In - F(ab')_2 ZCE-025 and 34% (25/74) with ^{111}In -ZCE-025. The use of MoAb fragments seems to be one

way of improving RIS⁽¹⁵⁾.

As has been pointed out by many workers, when ^{111}In is used as a radionuclide for labeling, high uptake by the normal liver tissue is the main drawback of RIS, making positive visualization of metastatic lesions in the liver difficult in many cases. However, introduction of the SPECT technique to this field has permitted positive visualization of such intrahepatic lesions. In our series, for example, the sensitivity for liver lesions increased from 8.7% (2/23) to 30.4% (7/23) by adding SPECT.

In our study, we did not investigate the relationship between the uptake of radio-labeled MoAb and tumor differentiation. However, Granowska et al.⁽⁶⁾ reported that there was an approximately thirteen times greater uptake by moderately and well differentiated tumors compared with poorly differentiated ones in colorectal cancer patients using ^{111}In -labeled C46 MoAb against CEA.

It was reported that tumor-free lymph nodes had a greater uptake of anti-CEA monoclonal antibodies than tumor-involved nodes. Granowska et al.⁽⁶⁾ reported that normal lymph nodes incorporated ^{111}In anti-CEA MoAb (C46) at a rate of 6 times higher than tumor-involved nodes. Using an ^{111}In -labeled anti-CEA MoAb (T84.66), Beatty et al.⁽¹¹⁾ also reported a high concentration of ^{111}In -MoAb in normal lymph nodes in colorectal cancer patients; namely, $24.3 \pm 6.7\%$ ID/kg for normal lymph nodes, and $4.53 \pm 0.44\%$ ID/kg for tumor-involved nodes. In our study, histologically tumor-free nodes were frequently imaged, thereby called false positives. Although the mechanism of trapping CEA by normal nodes is not fully understood, the immediate importance of this observation is that it is difficult to stage colorectal cancer by RIS using the anti-CEA monoclonal antibody.

The skin test was negative for all 24 patients. Although very mild urticaria and pruritus in one patient and very mild urticaria in a second patient were documented, no remarkable changes in the vital signs, hematological findings, serum biochemical profiles or urinalysis were observed. Administration of 42 mg of ZCE-025 can be considered safe.

Formation of HAMA was observed in all 21 patients examined. In the earliest case, HAMA was formed at about one week after MoAb administration, and in the latest case it was observed after six weeks. Once HAMA

was formed, it persisted for more than 30 weeks. When patients with a high titer of HAMA receive murine MoAb infusion, it is expected that murine MoAb and HAMA form complexes which result in rapid clearance of the radioactivity, high liver uptake and low tumor uptake of the murine MoAb¹⁶⁾. The formation of HAMA means that care should be taken in the event of repeated use of ^{111}In -ZCE-025 for monitoring of postsurgical recurrence. This problem may be overcome by the application of a human MoAb or a genetically engineered murine/human chimeric MoAb^{17),18)}.

Fifteen of 16 specimens resected from tumors of the colon and rectum were positive for immunohistochemical staining. The one negative lesion was depicted by RIS. This may be attributable to the heterogeneity of CEA distribution in the tumor mass. Ten of 14 normal colon and rectal specimens were positive for immunohistochemical staining. In this respect, Fritsche et al.¹⁹⁾ and Ahnen et al.²⁰⁾ also confirmed the presence of CEA in normal colon tissues.

In conclusion, this method can perfectly depict the primary lesions and local recurrence of colorectal cancers, therefore, may be useful for preoperative screening and diagnosis of local recurrence. But the formation of HAMA should be taken into consideration when this method is repeatedly used. At present, for metastatic foci in the lymph nodes, this method possesses only a complementary role.

This study was conducted as a joint research project:

Chairman: K. Hojo; Vice-chairman: H. Oyamada.

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要 旨

大腸・直腸癌の診断における ^{111}In 標識抗 CEA モノクローナル抗体
(^{111}In -ZCE-025) の I/II 相試験について

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^{111}In 標識マウスモノクローナル抗体 (ZCE-025) についての I/II 相臨床試験が, 国内 5 施設の協同研究の形で大腸・直腸癌患者 24 例を対象に実施された。そのうち, 評価可能とされた 22 例についてみると, 原発巣および局所再発巣はすべて描出された (21/21) が, リンパ節に関しては false positive が多かった。本法は原発巣や術後の再発巣の診断には有用であるが, リンパ節転移の診断には限界があると思われた。