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Title Page

A phase I trial of SGN-CD70A in patients with CD70-positive metastatic renal cell carcinoma

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Precis: In this study we examined safety of the new drug SGN-CD70A in metastatic kidney cancer. We found that it had a reasonable safety profile at lower dose levels and modest effect in stabilizing tumors.

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Conflicts of Interest

Sumanta K Pal reports consulting roles with Genentech, Aveo, Eisai, Roche, Pfizer, Novartis, Exelixis, Ipsen, BMS, Astellas, and honoraria from Genentech.

Nicholas Vogelzang reports:

Speaker's Bureau: Pfizer [Kidney cancer (Sunitinib, axitinib)]; Bayer [Prostate cancer (Radium 223)]; Novartis [Kidney cancer, PNET (Pazopanib, everolimus); Sanofi [Prostate cancer (Cabazitaxel)], BMS [Kidney cancer (BMS-nivolumab)]; Genentech/Roche [Bladder cancer (Atezolizumab); Astra Zeneca {Bladder cancer (durvalumab)].

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Andres Forero-Torres reports:
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John C Morris reports:
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John A. Thompson reports:
Advisory Boards: Seattle Genetics

Thomas Boyd reports:
Advisory Boards: Celgene
Travel Expenses: Celgene, Juno
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Christopher Hoimes reports:
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Hong Li; Cindy Yu; Elaina M. Gartner, and Anne-Sophie Carret report employment by and equity ownership of Seattle Genetics, Inc.

Saurabh Chhabra, Paulo G. Bergerot, and Jacob J. Adashek report no conflicts of interest.

ABSTRACT

Background: CD70 is frequently expressed in renal cell carcinoma (RCC) and has immunomodulatory properties. An antibody-drug conjugate targeting CD70, SGN-CD70A, was developed to treat CD70-positive RCC.

Methods: The objective of this phase I, open-label, dose-escalation, multicenter study was to evaluate the safety and tolerability of SGN-CD70A and establish its maximum tolerated dose (MTD) in CD70-positive metastatic RCC (mRCC). All subtypes of RCC were permitted, and no limit was set on number of prior therapies. Safety assessments consisted of monitoring and recording of all adverse events (AE) and dose-limiting toxicities (DLT). Treatment response was assessed by radiographic tumor evaluation according to the Response Evaluation Criteria for Solid Tumors (RECIST) v. 1.1. Model-based modified continual reassessment method (mCRM) was used to estimate the probabilities of DLT and response.

Results: The MTD was determined to be 30 mcg/kg with thrombocytopenia as the DLT. The most common AEs were fatigue (67%), anemia (61%), and thrombocytopenia (56%). Of

18 enrolled patients, 1 and 13 achieved partial response and stable disease, respectively, for a clinical benefit rate of 78%. Limitations of the study include the heavily pretreated nature of patients; a median of 4 prior lines of therapy were received (range: 1-8), diminishing response potential.

Conclusions: The modest antitumor activity of SGN-CD70A does not support development in mRCC. However, given the high disease control rate in a heavily pretreated population and modest toxicity profile, CD70 remains of interest due to its immunomodulatory properties.

INTRODUCTION

Management of metastatic renal cell carcinoma (mRCC) has evolved markedly over the course of the past several years. While vascular endothelial growth factor (VEGF)-directed therapies such as sunitinib and pazopanib have represented a first-line standard for over a decade, these therapies are being quickly supplanted by combinations utilizing immunotherapies[1]. Specifically, the CheckMate214 trial showed an improvement in overall survival (OS) using dual checkpoint inhibition with nivolumab and ipilimumab versus sunitinib monotherapy, and this combination was recently approved by the FDA[2]. The recently reported Immotion151 trial compared combined VEGF and checkpoint inhibition with bevacizumab and atezolizumab to sunitinib[3]. This study also met its initial primary endpoint, showing an improvement in progression-free survival (PFS) in a programmed death-ligand 1 (PD-L1) positive population.

With doublet therapies being used in the first line setting, particularly combinations of VEGF and immune checkpoint inhibitors, patients who are not cured with these therapies are left with very few options. All other approved therapies for mRCC function by abrogating signaling through VEGF or its downstream mediator, the mammalian target of rapamycin (mTOR). There is therefore a need for novel therapies that are mechanistically distinct. Cytotoxic agents have not traditionally been active for mRCC, but an agent that exploits a unique target in this disease, delivering a cytotoxic molecule to mRCC cells, may be beneficial. To this end, we have examined CD70, a target expressed on tumor cells of a wide variety of malignancies including, but not limited to, Hodgkin lymphoma, non-Hodgkin lymphoma (NHL), renal cell carcinoma (RCC), pancreatic cancer, ovarian cancer, lung cancer, and breast cancer[4-6]. In a series of 283 patients with RCC, we identified that 72% had increased CD70 expression[7]. Rates of expression were highest (82%) amongst 230 patients with confirmed clear cell histology.

The exact role of CD70 in RCC pathogenesis is unknown; however, there is evidence to suggest that the interaction between CD70 and CD27 may allow the tumor to escape immune responses through a decrease in the effector T cell/regulatory T cell ratio[8]. In this paper, we report the results of the first-in-human, phase I study of antibody-drug conjugate (ADC) SGN-CD70A directed against the CD70 antigen in patients with mRCC. The cytotoxic component of SGN CD70A is a DNA-crosslinking pyrrolobenzodiazepine (PBD) dimer drug, which initiates cellular events leading to double strand breaks and eventual cellular apoptosis[9].

PATIENTS AND METHODS

Patient Eligibility

This phase I, dose-escalation study (NCT02216890) was designed to evaluate the safety and tolerability of SGN-CD70A and to establish the maximum tolerated dose (MTD) in patients with mRCC and NHL. The current manuscript reports only outcomes for patients with mRCC; outcomes for patients with NHL will be reported separately. Ten centers in the United States recruited patients between June 2015 and July 2016, under approval by an Institutional Review Board in accordance with the Declaration of Helsinki. All patients provided informed consent prior to administration of any study treatment. Eligible patients had a pathologically confirmed diagnosis of CD70-positive RCC as determined by central review (defined as expression in at least 50% of the sample) with radiographic evidence of metastatic disease. All histologic subtypes were permitted and there was no limit on prior therapies, with the exception of prior anti-CD70-directed therapy. Patients had to have received at least two prior systemic therapies for metastatic disease, including receptor tyrosine kinase inhibitor (TKIs) and/or mTOR inhibitors. Patients were aged 18 years or older with an Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1, with adequate baseline renal, hepatic, and bone marrow function, including platelet count ≥100,000/μL

Study Design and Treatment

SGN-CD70A was administered intravenously on day 1 of 6-week cycles. The study initiated with a 3-week cycle dosing schedule; however, due to observations of prolonged thrombocytopenia in patients with NHL, the dosing schedule was changed to every 6 weeks to allow the bone marrow sufficient time to recover between doses. Patients were evaluated for response after every cycle of treatment for the first six cycles, then every two cycles according to the Response Evaluation Criteria for Solid Tumors (RECIST) Version 1.1[10]. Patients who achieved stable disease (SD) or better were eligible to continue receiving study treatment until disease progression or unacceptable toxicity. Patients who discontinued study treatment prior to disease progression were evaluated for response until progression or initiation of new anticancer treatment, whichever occurred first.

This study was conducted using a model-based modified continual reassessment method (mCRM) statistical design that implemented Bayesian methodology to estimate the probabilities of dose limiting toxicity (DLT) and response at each dose level. The dose-toxicity and dose-response relationship were modeled separately for each arm (mRCC or NHL), and the MTD

was determined separately for each arm. Dose levels for dose escalation were 8 (NHL Arm starting dose; not tested for RCC patients), 15, 30, 50, 80, 120, 160, and 200 mcg/kg.

Study Assessments

Non-standard safety assessments in this study included serial electrocardiograms, pulmonary monitoring (pulmonary function tests), and renal monitoring (routine urinalysis with reflexive microscopy, creatinine clearance, and urine protein:creatinine [UPC] calculation/24 hr local assessments every three weeks). Treatment response was assessed by radiographic tumor evaluation at protocol-specified timepoints. Spiral computed tomography (CT) scans of chest, abdomen, and pelvis were obtained. Bone scans or fluorodeoxyglucose (FDG)-positron emission tomography (PET) scans had to be performed to follow bone metastasis, if appropriate. Investigator assessments of clinical progression without imaging were also allowed.

Pharmacokinetic (PK), Pharmacodynamic, and Immunogenicity Assessments

Blood samples for SGN-CD70A PK analysis were collected predose, within 15 minutes after the end of infusion; and 2, 6, and 24 hours, and 3, 7, 14, 21 and 28 days from the start of infusion in Cycles 1, 2, and 4. Samples were collected only predose and within 15 minutes after the end of infusion in other cycles, and the end of treatment (EOT) visit. Blood samples for assessing the presence of anti-therapeutic antibody (ATA) were collected predose on day 1 of the first 5 cycles and every fifth cycle thereafter, and at the EOT visit.

Sensitive, qualified assays were used to measure concentrations of ADC (SGN-CD70A), total antibody (TAb), and released-free drug, PBD, in plasma, and ATA in serum. The assays included enzyme-linked immunosorbent assays (ELISA) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) assays. The limits of quantification for ADC, TAb, and PBD were 2.89 ng/mL, 2.93 ng/mL, and 10 pg/mL, respectively. Pharmacokinetic parameters were estimated by non-compartmental analysis using Phoenix® WinNonlin® v6·3 (Certara, Princeton, NJ). Blood samples were collected throughout the study to evaluate immune responses as appropriate.

Statistical Analysis

The primary objective was to evaluate the safety and tolerability of treatment with SGN-CD70A and to identify the MTD of SGN-CD70A in patients with CD70-positive RCC. The model-predicted MTD was the highest dose that had an estimated DLT rate less than 30%. The final MTD determination was made by the Safety Monitoring Committee (SMC), based on the estimated DLT rate provided by the model and cumulative safety information. Safety endpoints included the type, incidence, severity, seriousness, and relatedness of adverse events (AE) and

laboratory abnormalities. The pharmacokinetics of SGN-CD70A antibody-drug conjugate, TAb, and PBD (when measurable) were evaluated by noncompartmental analysis and summarized by descriptive statistics at each PK sampling time. ATA incidence rate was defined as the proportion of patients that developed ATA at any time during the study.

RESULTS

Patients

A total of 18 patients with mRCC were enrolled and treated in the study. The median age was 64 years (range 47 to 74). Most patients had the clear cell (94%) subtype of RCC at study entry. Additional demographic and disease characteristics are presented in Table 1. The reasons for discontinuation from study were progressive disease (10 patients [56%]), AE (5 patients [28%]), and non-AE-related patient decision (3 patients [17%]).

Safety

Adverse events considered to be DLTs are displayed by dose in Table 2. The DLTs encountered for RCC patients in this study were thrombocytopenia events. One DLT of Grade 3 thrombocytopenia (30 mcg/kg cohort) reported on study day 16 in Cycle 1 recovered to Grade 1 by study day 51. Two other DLTs of Grade 4 thrombocytopenia (50 mcg/kg cohort) reported on study day 15 and day 22 in Cycle 1 recovered to Grade 1 by study day 22 and Grade 2 by study day 29, respectively. In addition to two DLTs at 50 mcg/kg, it was noted that patients experienced difficulty tolerating ≥2 cycles of treatment at this dose due to edema and/or slow platelet recovery. Given this observation, the SMC recommended not assigning any further patients to treatment at this dose level. The MTD for mRCC population was determined to be 30 mcg/kg. Dose levels above 50 mcg/kg were not tested.

Of the 18 RCC patients, 94% experienced at least one treatment-emergent AE (TEAE). TEAEs observed in >20% of all treated patients are listed in Table 3. Treatment-related TEAEs occurring in >20% of patients were thrombocytopenia (56%), anaemia and fatigue (44% each), and peripheral edema (33%). Overall, 15 patients (83%) had at least one TEAE of at least Grade 3 severity. Grade 3 TEAEs that occurred in >10% of patients were thrombocytopenia (22%), anemia (17%), neutropenia (17%), and dehydration (11%). There were no reports of neutropenic fever.

Across the study, four of 18 mRCC patients (22%) had died at the time of study closure, none within 30 days of last dose. Five patients (28%) discontinued the treatment due to AEs. Two patients (11%) discontinued due to thrombocytopenia (Grade 2 and 4); the other three patients each discontinued due to abdominal pain (Grade 3), fatigue, and peripheral edema

(both of Grade 2). Two patients (11%) had an AE of thrombocytopenia and one patient (6%) had an AE of neutropenia that led to dose reduction of the investigational product.
There were 17 TEAEs of thrombocytopenia. Of these, 10 (59%) recovered with median time to resolution of 3.6 weeks. Median follow up time for unresolved thrombocytopenia was 13 weeks. Two patients experienced Grade 1 epistaxis during Grade 1/2 thrombocytopenia events. There were no other bleeding events reported.

There were eight patients (44%) who reported treatment-emergent edema. One of these patients in the 30 mcg/kg cohort experienced both generalized edema (Grade 3; duration of 9 days) and simultaneous gastrointestinal edema (Grade 2). This patient also experienced hypoalbuminemia (Grade 2) 12 days earlier that was ongoing during edema. No patient had dose reduction due to edema.

Efficacy

The best clinical response observed at all dose levels is displayed in Table 4. One patient in the 50 mcg/kg achieved a partial response (PR; 6%), with a time to first response of 18.4 weeks and duration of response of 7.3+ weeks (Figure 4). The majority of patients (13/18, 72%) had SD yielding an overall disease control rate (DCR) of 78% (95% CI: 52.4-93.6). Tumor size post treatment is shown in Figure 1. Interestingly, two patients (1 patient with PR and 1 patient with SD) in the 50 mcg/kg cohort had ongoing tumor reduction more than six weeks after the end of treatment (2 doses received in both cases). Both patients experienced Grade 2 thrombocytopenia, persistent in one case. Estimated median PFS was 3.5 months (95% CI: 2.1-6.3) (Figure 2). Four patients are known to have died and 14 patients were still alive at last follow-up, including the patient with PR. The follow up time for those who were still alive at last follow up ranged from 1.4+ to 9.7+ months. Two patients who died were known to have survived 17.6 and 14.1 months with best response of SD. Prior immunotherapy with PD-1/PD-L1 inhibitors was rendered in 4 patients (22.2%). The patient who derived a PR was not amongst these patients, however.

Pharmacokinetics and Immunogenicity

Pharmacokinetic parameters are summarized in Table 5. Following IV SGN-CD70A administration, plasma ADC concentrations appeared to decrease bi-exponentially with the mean terminal half-life ($t_{1/2}$) between four and five days across the 15-50 mcg/kg Q6W dose levels (Figure 3). After the first dose, the plasma ADC end-of-infusion concentration (C_{eoi}) and exposure (AUC_{inf}) were approximately dose-proportional. There was minimum accumulation across cycles as the geometric mean of accumulation ratio was approximately 1.0 for $AUC_{0\text{-}42d}$.

Plasma TAb concentration-time profiles were similar to those of the ADC but the exposure of TAb was generally slightly higher. Plasma levels of the unconjugated cytotoxic agent, PBD, were below the lower limit of quantification (10 pg/mL) in all samples obtained from all patients at dose levels of 15-50 mcg/kg, except for a single sample (26.6 pg/mL) from one patient 2 hours following a 30 mcg/kg SGN-CD70A dose.

Among treated patients (N = 18), ATA data were available for 15 patients (83%). None of them tested positive for anti-SGN-CD70A antibody at any visit during the study.

DISCUSSION

The current study identified modest single-agent activity with SGN-CD70A in patients with mRCC, with 1 patient achieving partial response and 13 patients achieving stable disease amongst 18 patients enrolled. While there is minimal response seen in this dataset, the majority of patients derived clinical benefit. Therefore, CD70 remains an interesting target for potential future RCC therapies.

The most common drug-related TEAEs of SGN-CD70A were thrombocytopenia, fatigue, anemia, and peripheral edema. Several biomarkers were examined to determine the cause for severity and duration of observed thrombocytopenia in the absence of other significant myelosuppression, including evaluation of IgG antibody and thrombopoetin (TPO) levels. Neither of these analyses correlated with occurrence or degree of thrombocytopenia (unpublished data). Additionally, CD70 is not known to be expressed on megakaryocytes or their precursors. While fatigue and anemia are common cancer-related symptoms, the rate of edema-related events was unexpected. The mechanism for edema is unclear. Mechanistic studies in immune thrombocytopenia (ITP) suggest that CD70, if anything, may be involved in platelet destruction[11]. Thus, an anti-CD70 directed therapy would not be anticipated to cause thrombocytopenia. It is possible, therefore, that the heavily pretreated nature of the patient population may account for the rates of thrombocytopenia (i.e., it could be disease related).

Modest activity was seen with SGN-CD70A monotherapy. Multiple factors may account for this, but the most important may be the extensive pre-treatment of patients in the current study. Patients had received a median of 4 lines of prior therapy, ranging from 1 to 8 prior treatments. There is a clear diminution of antitumor activity seen across lines of therapy for mRCC. In the front-line setting, PFS for most VEGF-directed therapies (e.g., sunitinib or pazopanib) ranges from 9-11 months[12, 13]. PFS with preferred agents in the second-line setting varies, but may be as high as 7-8 months with agents such as cabozantinib[14].Trials in the third-line setting have yielded much more limited results – the phase III experience comparing dovitinib (a non-

selective FGFR inhibitor) versus sorafenib yielded a PFS in the 3-4 month range[15]. In the current study, SGN-CD70A was applied essentially as fifth-line therapy.

Another important element to consider in this biomarker-based study is the potential effect of tumor heterogeneity. Our prior data indicates CD70 expression in upwards of 70% of patients with mRCC. However, it is unknown whether there is discordance in CD70 expression between primary and metastatic sites, or whether CD70 expression changes during the course of therapy. Multiple studies have suggested substantial genomic heterogeneity between primary and metastatic sites in RCC, with few ubiquitous mutations and multiple "private" mutations (e.g., mutations exclusive to single sites of disease)[16, 17].

A potential future anti-CD70 therapy may be of interest either as monotherapy or in combination with emerging immunotherapeutic agents. There is evidence that CD70 may play a role in T-cell trafficking and myeloid-derived suppressor cell (MDSC) recruitment[8]. Currently, the only front line immunotherapy combination with demonstrated benefit in a phase III trial in mRCC is nivolumab with ipilimumab, a PD-1 and CTLA-4 inhibitor, respectively[2]. However, trials combining PD-1/L1 inhibitors with novel immunotherapeutic strategies (e.g., CD-122-based agonist NKTR-214) are moving forward[18]. These studies show high response rates, implying synergy with the approach of dual immune targeting, and also appear to offer less toxicity than the combination of PD-1/L1 and CTLA-4 blockade.

In summary, there are certain factors (e.g., extent of prior therapy, tumor heterogeneity) that could account for the modest clinical activity seen with SGN-CD70A. Given the immunomodulatory properties of the compound, CD70 remains an interesting target for potential future RCC therapies in combination with emerging therapeutic agents.

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TABLES AND FIGURES

Figure Legends

Figure 1: Tumor Size Over Time (N=18)

Diamond indicates response assessment that occurred after the last dose.
EOT = end of treatment; CP = clinical progression; PD = progressive disease; PR = partial response; SD = stable disease.

Figure 2: Median PFS in Patients with mRCC Receiving SGN-CD70A (N=18)

CI = confidence interval; mRCC = metastatic renal cell carcinoma; PD = progressive disease; PFS = progression free survival.

Figure 3: First-dose Antibody Drug Conjugate mean concentration-time profile for patients treated with SGN-CD70A

Figure 4: Partial response to SGN-CD70A in a patient with mRCC. Pre-treatment (a) and post-treatment (b) images indicate tumor reductions in pulmonary (top panel) and gluteal (bottom panel) lesions.

Table 1: Patient Characteristics

Median age (range), y	64 (47-74)
Sex, male, No. (%)	18 (100)
Race, white, No. (%)	18 (100)
ECOG performance[a], No. (%)	
0	10 (56)
1	8 (44)
Renal cell carcinoma diagnosis subtype, No. (%)	
Clear Cell	17 (94)
TFE3 Translocation	1 (6)
Number of prior systemic therapies per patient	
Median (range)	4 (1-8)

a Values for ECOG performance status range from 0 to 5, with higher scores indicating greater disability.
ECOG = Eastern Cooperative Oncology Group.

Table 2: Dose-Limiting Toxicities in mRCC Patients

	15 mcg/kg (N=3) n (%)	**30 mcg/kg (N=7) n (%)**	**50 mcg/kg (N=8) n (%)**	**Total (N=18) n (%)**
Thrombocytopenia/Platelet count decreased	0	1 (14)	2 (25)	3 (17)

	15 mcg/kg (N=3) n (%)	30 mcg/kg (N=7) n (%)	50 mcg/kg (N=8) n (%)	Total (N=18) n (%)
DLT rates and probability				
DLT rate (SD)	10.2% (0.064)	14.3% (0.072)	23.0% (0.114)	-
Model-based probability of DLT rate < 30%	0.988	0.968	0.748	-

DLT = dose-limiting toxicity; mRCC = metastatic renal cell carcinoma; SD = standard deviation.

Table 3: Summary of Adverse Events in mRCC Patients

	15 mcg/kg (N=3) n (%)	30 mcg/kg (N=7) n (%)	50 mcg/kg (N=8) n (%)	Total (N=18) n (%)
Fatigue	2 (67)	2 (29)	8 (100)	12 (67)
Anemia	2 (67)	4 (57)	5 (63)	11 (61)
Thrombocytopenia	1 (33)	3 (43)	6 (75)	10 (56)
Arthralgia	2 (67)	4 (57)	1 (13)	7 (39)
Peripheral edema	1 (33)	2 (29)	4 (50)	7 (39)
Dyspnea	1 (33)	1 (14)	4 (50)	6 (33)
Nausea	0	1 (14)	4 (50)	5 (28)
Abdominal pain	0	1 (14)	3 (38)	4 (22)
Increased blood alkaline phosphatase	0	1 (14)	3 (38)	4 (22)
Dehydration	0	1 (14)	3 (38)	4 (22)
Hypoalbuminemia	0	1 (14)	3 (38)	4 (22)
Pain in extremity	0	2 (29)	2 (25)	4 (22)
Pleural effusion	1 (33)	2 (29)	1 (13)	4 (22)
Pyrexia	1 (33)	0	3 (38)	4 (22)
Vomiting	0	2 (29)	2 (25)	4 (22)

mRCC = metastatic renal cell carcinoma.

	15 mcg/kg (N=3)	30 mcg/kg (N=7)	50 mcg/kg (N=8)

Table 4: Summary of Responses in mRCC Patients

	15 mcg/kg (N=3) n (%)	30 mcg/kg (N=7) n (%)	50 mcg/kg (N=8) n (%)	Total (N=18) n (%)
Best Clinical Response[a]				
Partial Response (PR)	0	0	1 (13)	1 (6)
Stable Disease (SD)	3 (100)	4 (57)	6 (75)	13 (72)
Progression	0	3 (43)	1 (13)	4 (22)
Progressive Disease (PD)	0	2 (29)	1 (13)	3 (17)
Clinical Progression (CP)[b]	0	1 (14)	0	1 (6)
ORR (CR + PR)	0	0	1 (13)	1 (6)
95% confidence interval[c] for ORR	(0.0, 70.8)	(0.0, 41.0)	(0.3, 52.7)	(0.1, 27.3)
DCR (CR+PR+SD)	3 (100)	4 (57)	7 (88)	14 (78)
95% confidence interval[c] for DCR	(29.2, 100.0)	(18.4, 90.1)	(47.3, 99.7)	(52.4, 93.6)

a Clinical response is defined according to RECIST v1.1.

b Patients with both PD and CP were counted as PD. Patients who could not be assessed or were assessed as better than PD according to RECIST, but had investigator claim of clinical progression at the same visit were counted as CP.

c Two-sided 95% exact confidence interval, calculated using the Clopper-Pearson method[19]

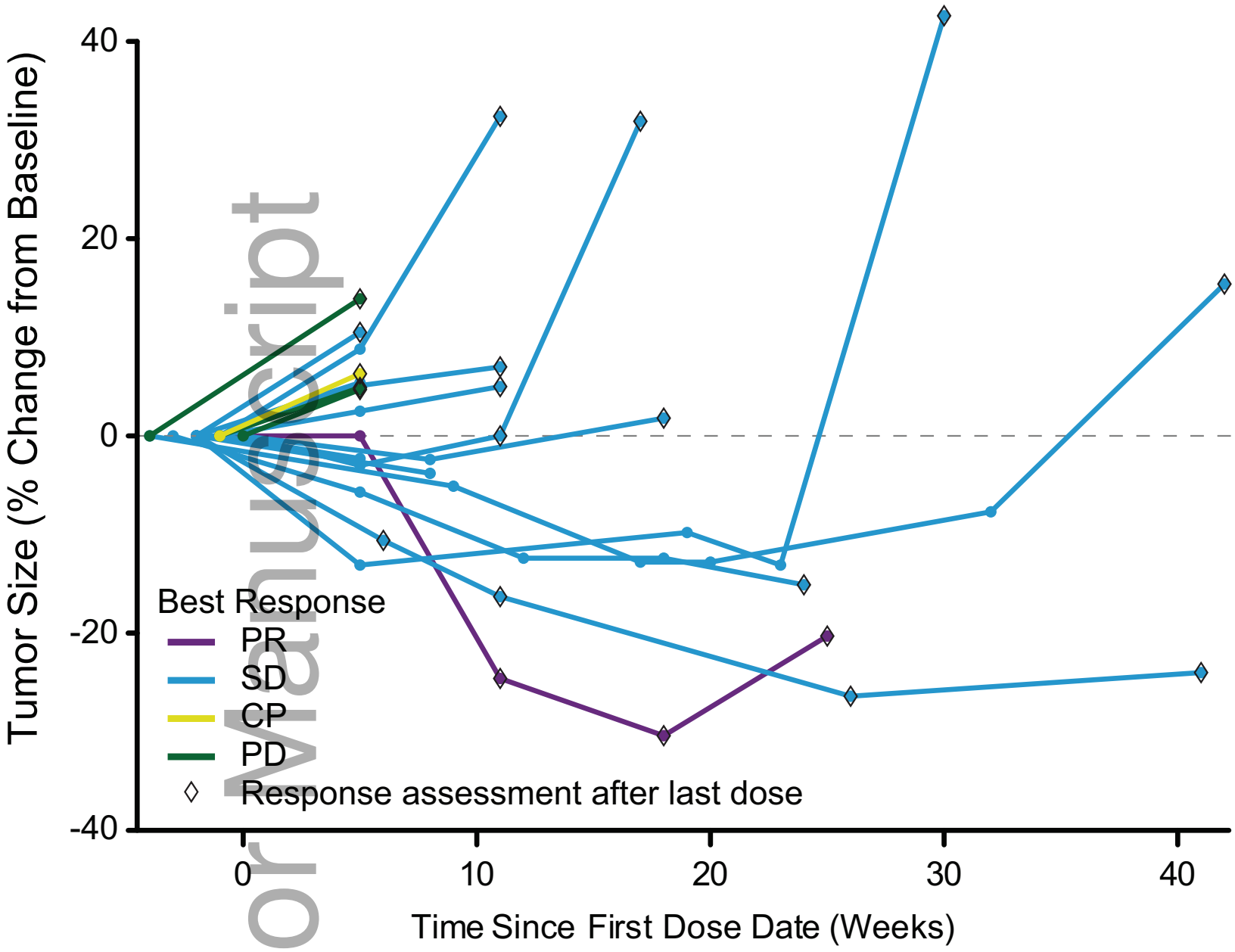
CR = complete response, DCR = disease control rate; mRCC = metastatic renal cell carcinoma; ORR = objective response rate; RECIST = Response Evaluation Criteria for Solid Tumors.

Table 5: First-Dose Pharmacokinetic Parameters for SGN-CD70A ADC and Tab

SGN-CD70A ADC			
$AUC_{0\text{-}42d}$ (ng*day/mL)	913.32 (46)	1545.99 (38)	2442.88 (44)
AUC_{inf} (ng*day/mL)	916.40 (46)	1549.15 (38)	2454.57 (43)
C_{eoi} (ng/mL)	294.00 (-)	720.22 (51)	1166.79 (38)
$t_{1/2}$ (days)	5.49 (6)	4.89 (21)	4.89 (34)
V_{ss} (mL)	7913.65 (44)	6796.59 (29)	8161.57 (28)
CL (mL/day)	1473.16 (64)	1592.13 (29)	1790.55 (28)
SGN-CD70A TAb			
$AUC_{0\text{-}42d}$ (ng*day/mL)	1190.78 (53)	2048.46 (47)	2642.13 (52)
C_{eoi} (ng/mL)	294.00 (-)	627.13 (25)	1064.67 (33)

Data are presented as geometric mean (% coefficient of variation).

ADC = antibody-drug conjugate; $AUC_{0\text{-}42d}$ = area under the curve from 0 to 42 days; AUC_{inf} = area under the curve from 0 to infinity; C_{eoi} = concentration at end of infusion; CL = clearance; $t_{1/2}$ = terminal half-life; TAb = total antibody; V_{ss} = volume of distribution at steady state.



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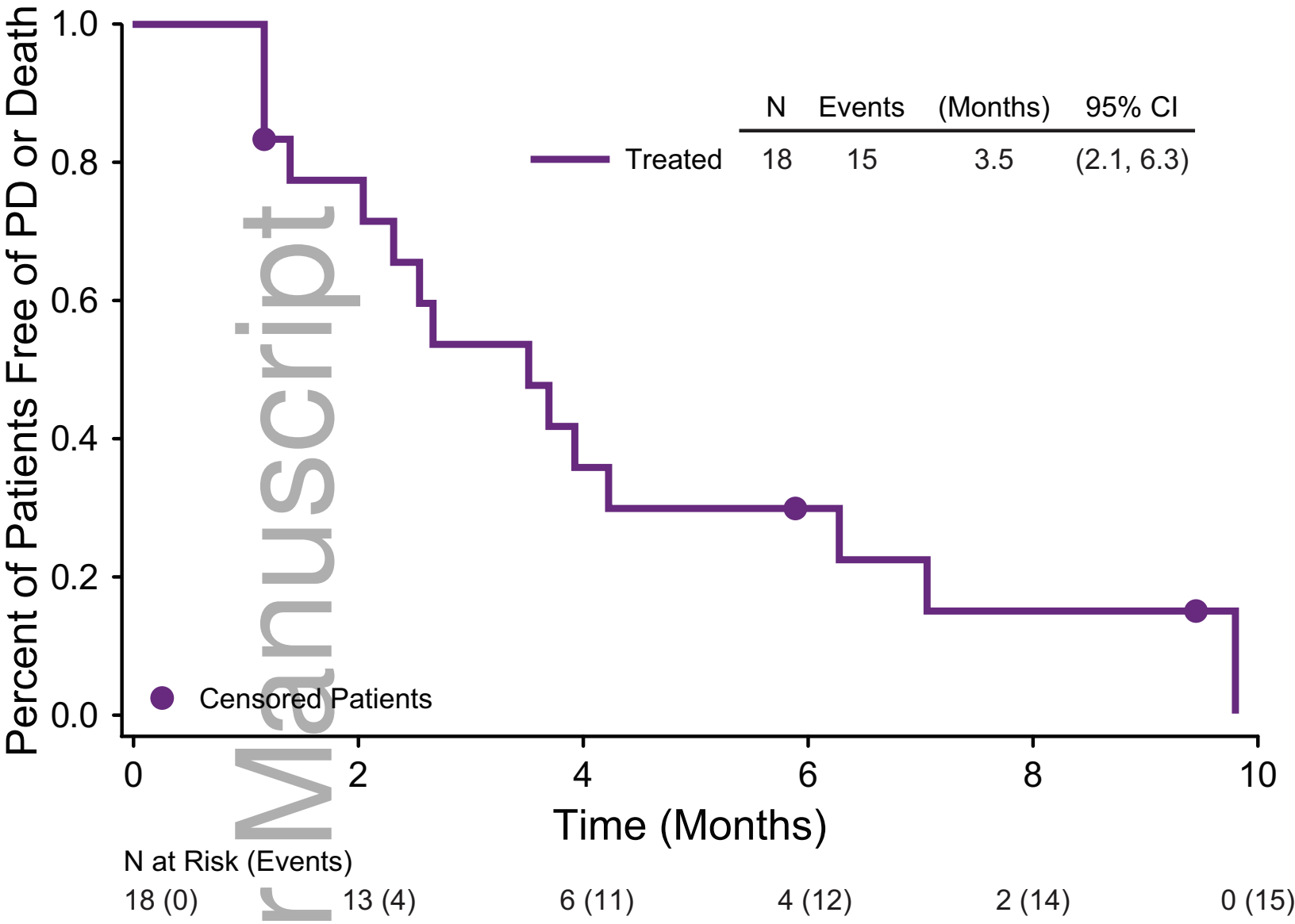

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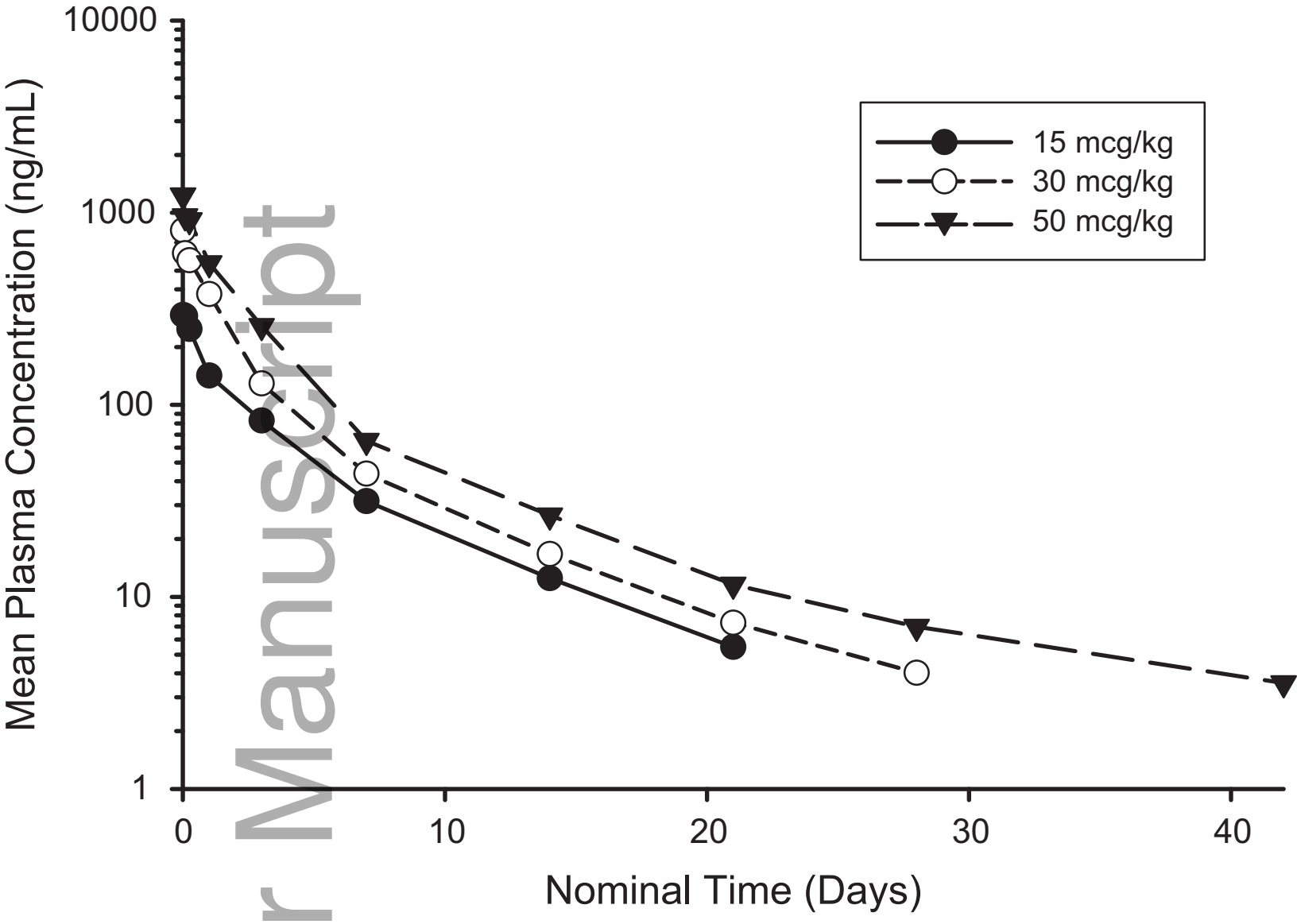

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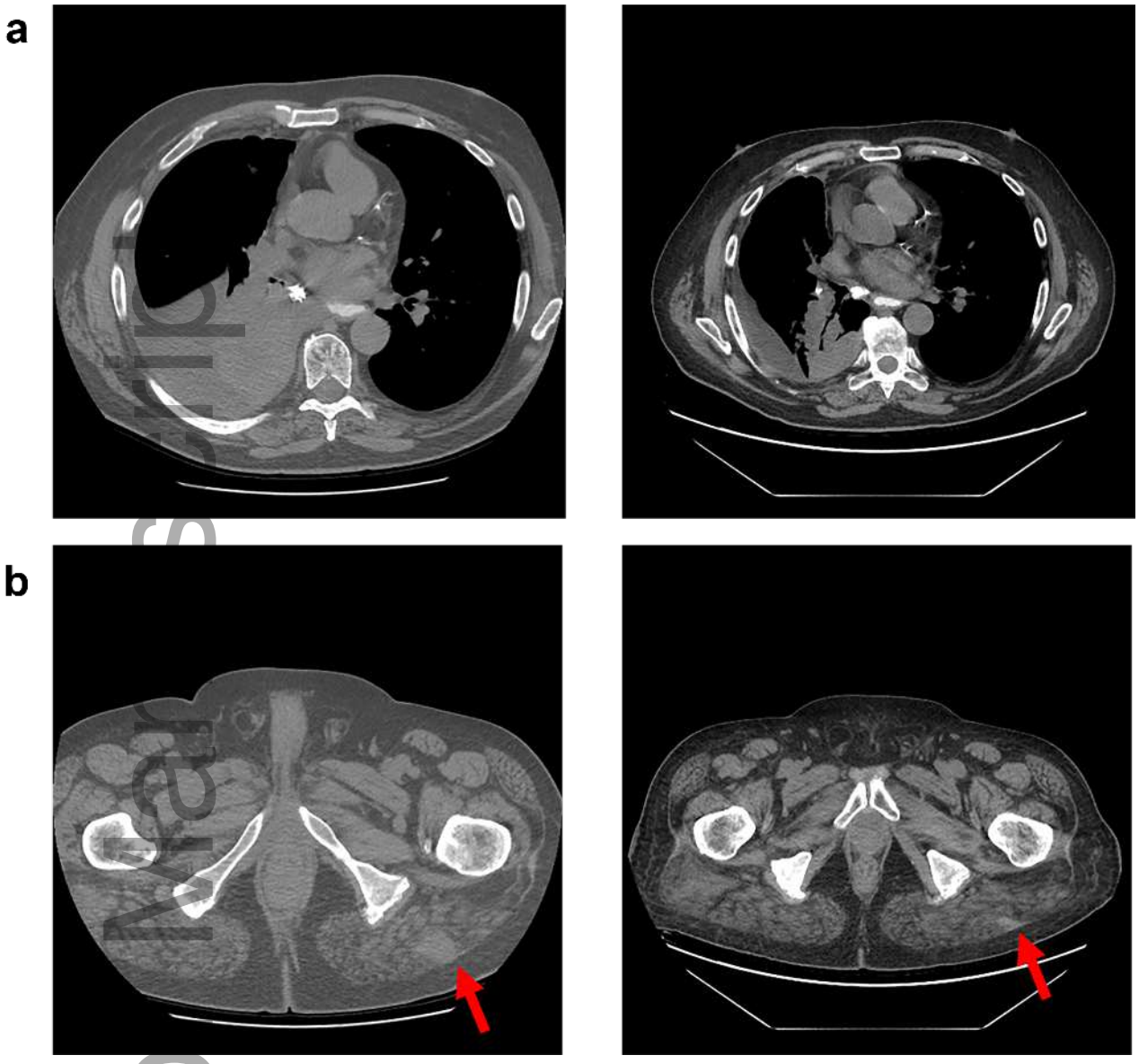

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