Real world experience of FGFR gene alterations and clinical outcomes in advanced/metastatic urothelial cancer in Japan: MONSTAR-SCREEN database study —UroCaMon—

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KEY TAKEAWAYS

Early detection of FGFR alteration may provide new insights on treatment sequence for patients with a/mUC, especially for those who benefit from FGFR inhibitors.

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CONCLUSIONS

- The results showed a similar trend compared to prior studies, suggesting the possibility of clinical application in Japan based on previous findings.
- No difference was found in the PFS and the estimated survival rate of FGFR2/3 GA-positive or –negative patients.
- Our data showed that treatment pressure may not alter the FGFR status.

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INTRODUCTION

- Gene alterations (GA) in fibroblast growth factor receptor (FGFR) may be oncogenic drivers in urothelial cancer (UC)
- The association between FGFR GA status and the prognosis with platinum-based chemotherapy is unknown in Asian patients
- This study aims to elucidate the proportion and prognosis of FGFR2 or 3 (2/3) GA-positive advanced or metastatic UC (a/m UC)

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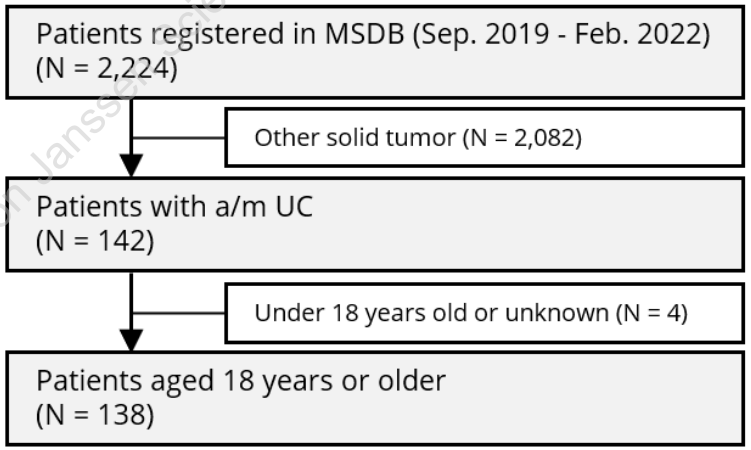
Data source

- MONSTAR SCREEN study1: 1) Genetic screening project by the National Cancer Center of Japan2, 2) Screening of genes over 2,000 advanced solid tumor patients other than Lung cancer, 3) Large volumes of prospective patient-level data on cancer biomarkers, patient clinical characteristics, anti-cancer treatment history, and longitudinal clinical outcomes
- MONSTAR SCREEN Database (MSDB): FoundationOneLiqid (F1L) was used for detecting 324 cancer-related genes, including FGFR
- Study patients: registered in MSDB

Patient flow



1) Yoshiaki Nakamura et al. Cancer Sci. 2021 Nov 112(11): 4425-4432. 2) Yoichi Fujii et al. Cancer Cell . 2021 Jun 14;39(6):793-809.e8

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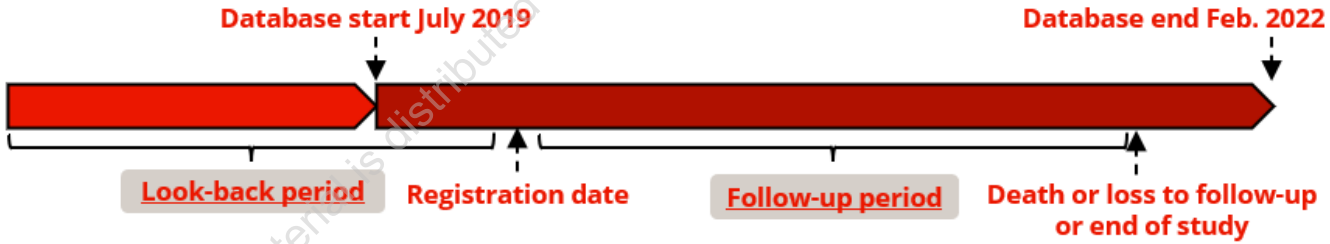
METHODS

FIGURE 1: Study design

- All patients: patients registered in MSDB between Sep. 2019 and Feb. 2022
- a/m UC patients: all patients with a/m UC and aged 18 years or older
- FGFR2/3 GA definition3: Amino acid variant (FGFR3); R248C, S249C, G370C, Y373C, Fusion variant; FGFR2-BICC1, FGFR2-CASP7, FGFR3-TACC3, FGFR3-BAIAP2L1
- Registration date: the date that the patient was registered in MSDB
- Look-back period: the period from diagnosis of a/m UC to registration
- Follow-up period: the period from the registration date to the subject's death, loss to follow-up, or the end date of the MSDB study, whichever comes first
- First-line treatment date: the initiation date of the patient's first-line treatment
- In the patient population, where the gene test results were used to make a decision, patients with a gene test of "Fail" only were excluded



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RESULTS

Table1: Patient characteristics in *FGFR2/3* GA

		Total n (%)	Positive n (%)	Negative n (%)
		N = 138	N = 16*	N = 119*
Sex	Male/Female	95/43	11/5	82/37
Age (years)	Median [range]	72.0 [42-90]	70.0 [50-86]	72.0 [42-90]
Age Category	18–64	30 (21.7)	3 (18.8)	25 (21.0)
	65–74	56 (40.6)	8 (50.0)	47 (39.5)
	75 or more	52 (37.7)	5 (31.3)	47 (39.5)
Smoking status/history	Yes	75 (54.3)	7 (43.8)	67 (56.3)
	No/Unknown	63 (45.7)	9 (56.3)	52 (43.7)
ECOG PS	0–1	90 (65.2)	9 (56.3)	79 (66.4)
	2–3	10 (7.2)	2 (12.5)	8 (6.7)
	Unknown	38 (27.5)	5 (31.3)	32 (26.9)
Primary tumor histopathology	Pure UC	102 (73.9)	13 (81.3)	88 (73.9)
	Non-Pure UC	12 (8.7)	2 (12.5)	10 (8.4)
Primary tumor site	Bladder	70 (50.7)	8 (50.0)	62 (52.1)
	Upper tract UC	68 (49.3)	8 (50.0)	57 (47.9)
TNM staging (N)	N0	69 (50.0)	8 (50.0)	59 (49.6)
	N1-N3, NX	67 (48.6)	8 (50.0)	58 (48.7)
	Unknown	2 (1.4)	0 (0.0)	2 (1.7)
TNM staging (M)	M0	96 (69.6)	11 (68.8)	83 (69.7)
	M1	40 (29.0)	5 (31.3)	34 (28.6)
	Unknown	2 (1.4)	0 (0.0)	2 (1.7)
No. of prior therapies	SACT (+)	22 (15.9)	2 (12.5)	20 (16.8)
	SACT (-)	52 (37.7)	6 (37.5)	44 (37.0)
Genetic testing method	F1L CDx	135 (97.8)	16 (100.0)	119 (100.0)
	F1 CDx	31 (22.5)	5 (31.3)	26 (21.8)
	Other	68 (49.3)	9 (56.3)	59 (49.6)
F1L CDx Count	1	84 (60.9)	10 (62.5)	74 (62.2)
	2 or more	51 (37.0)	6 (37.5)	45 (37.8)

ECOG PS; Eastern cooperative oncology group performance status,
F1; FoundationOne, SACT; systemic anti-cancer therapy TNM; Tumor, node and metastasis *Total of Positive/Negative: 3 patients of "Fail" in F1L were excluded TNM staging; test results as of the First-line treatment date

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Table 2: Proportion of *FGFR2/3* GA (+) pts.

		n (N = 135)	% (95%CI)
FGFR2/3 GA (+)		16	11.9 (6.9, 18.5)
Gene Mutation	AA variant		
FGFR3	R248C	2	1.5 (0.2, 5.2)
	S249C	6	4.4 (1.6, 9.4)
	G370C	0	0.0 (0.0, 2.7)
	Y373C	4	3.0 (0.8, 7.4)
	R248C & S249C†	1	0.7 (0.0, 4.1)
Fusion Gene	Fusion ID		
FGFR3	*FGFR3-TACC3*	5	3.7 (1.2, 8.4)

AA; Amino acid, pts; patients: †Cases with two variants *FGFR2* was not detected

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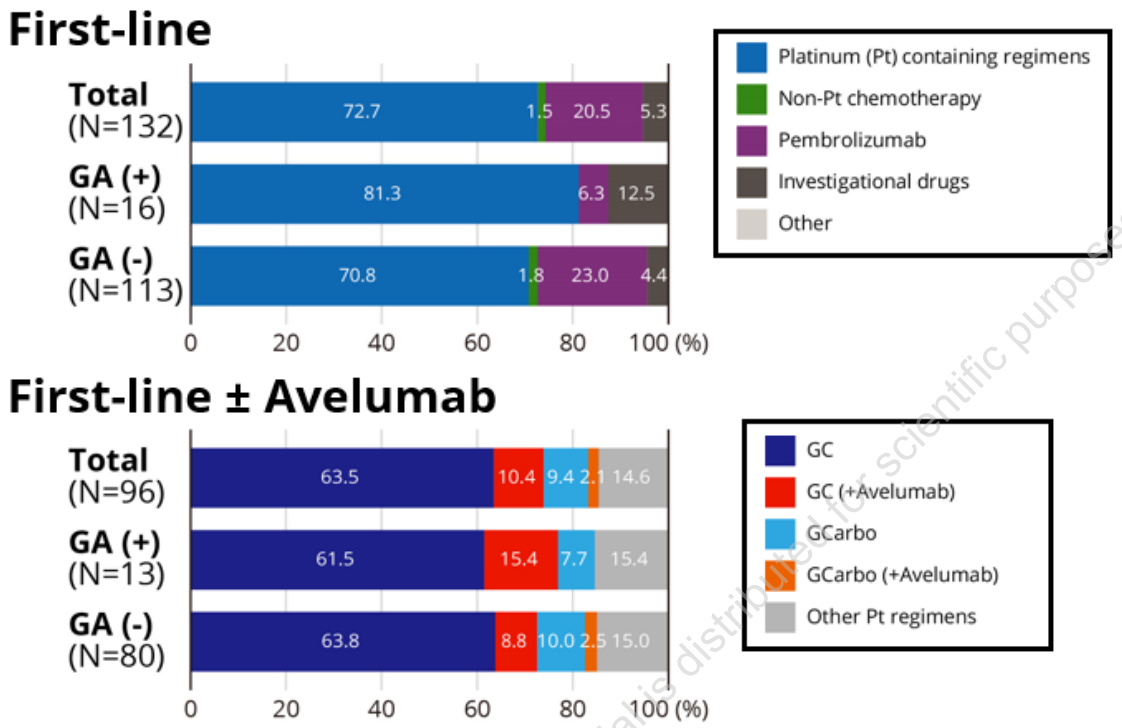
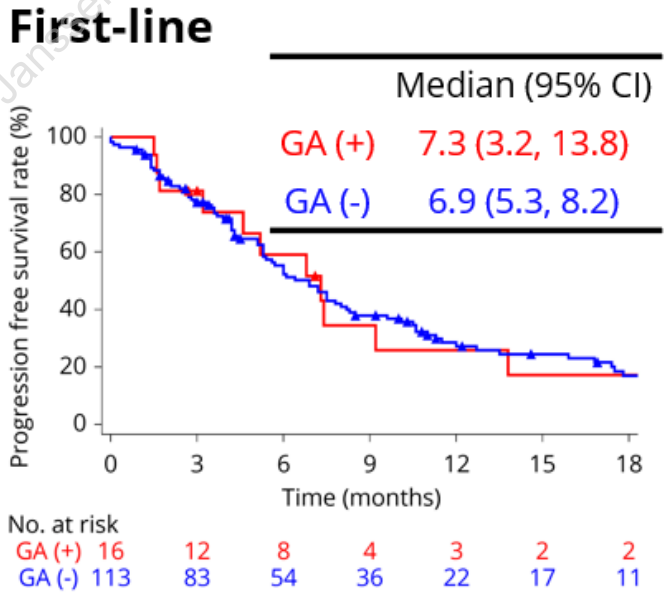
FIGURE 3, 4: Treatment patterns & Time to progression by each line of therapy in *FGFR2/3* GA





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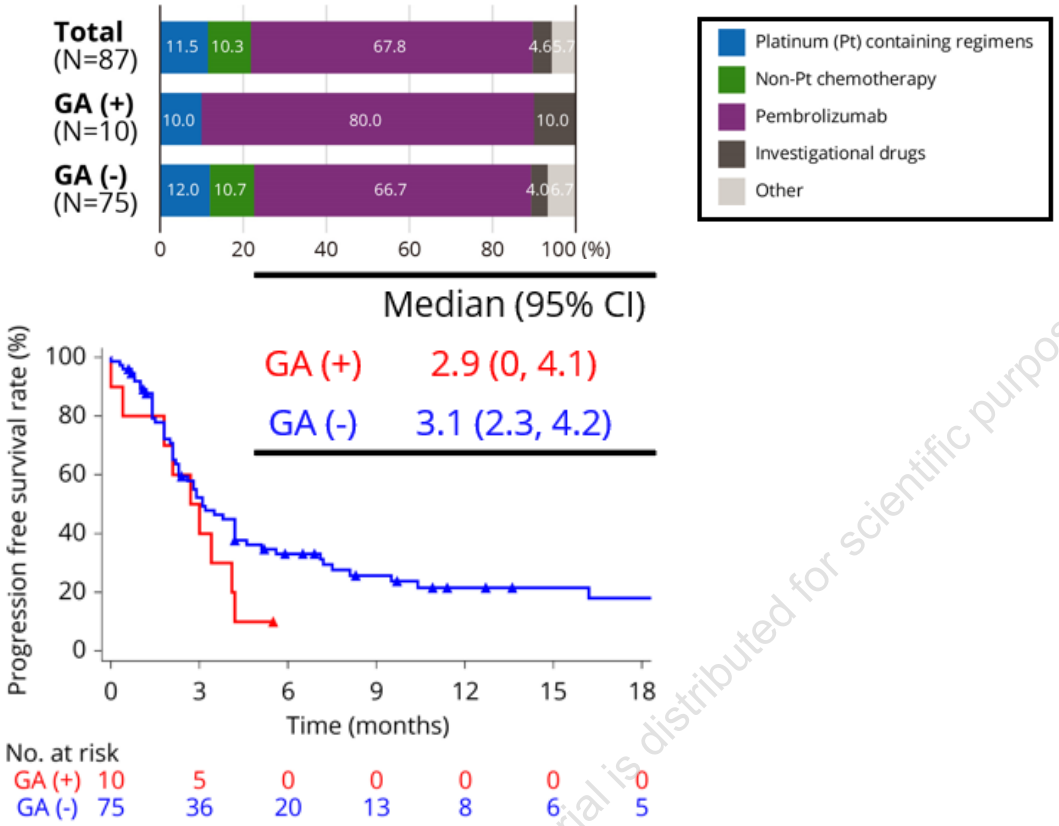
Second-line



Third-line

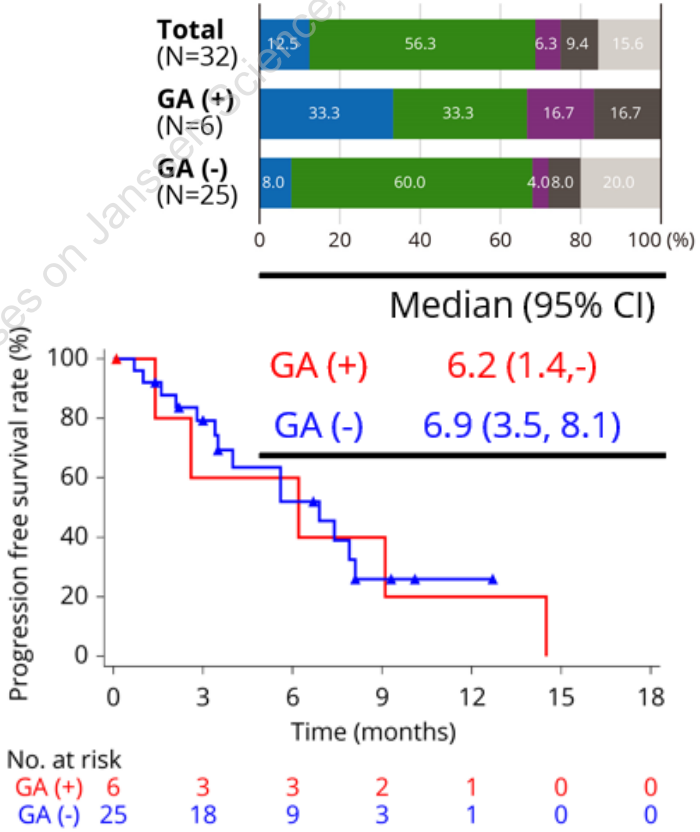


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Figure 5: Time to death (OS) of UC by first-line treatment and subgroups

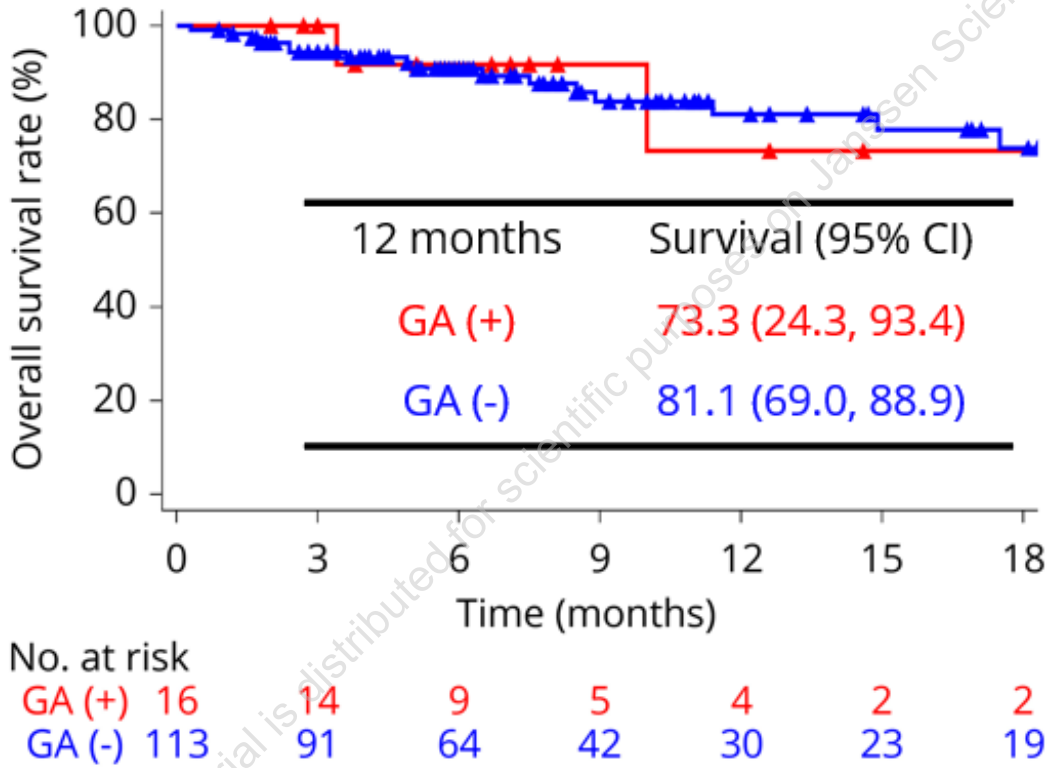

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Figure 6: Co-occurrence and mutual exclusivity plot for *FGFR* and other typical GA

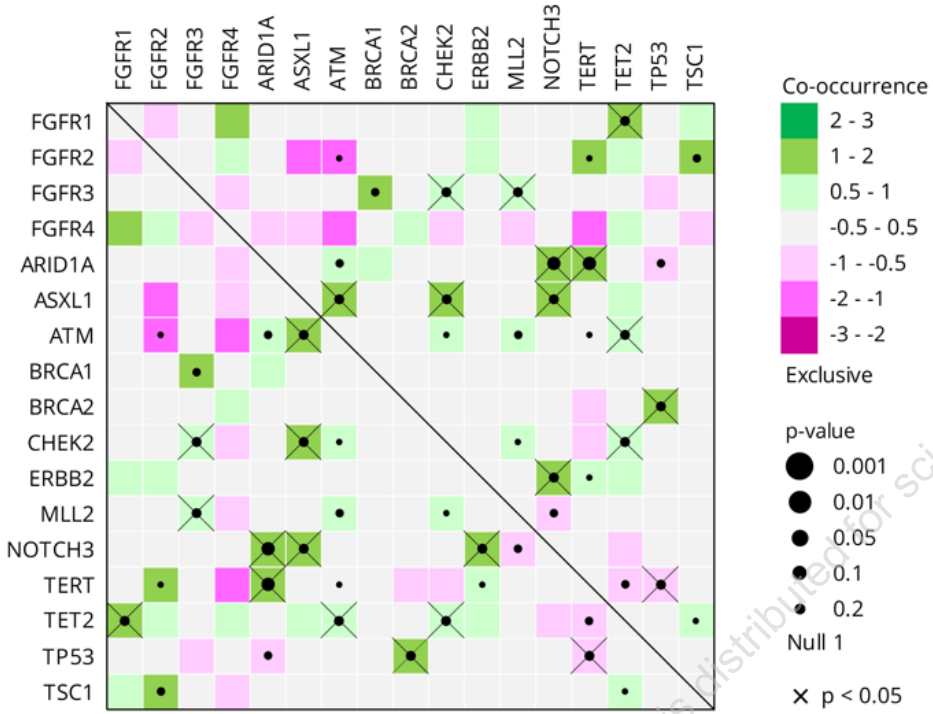
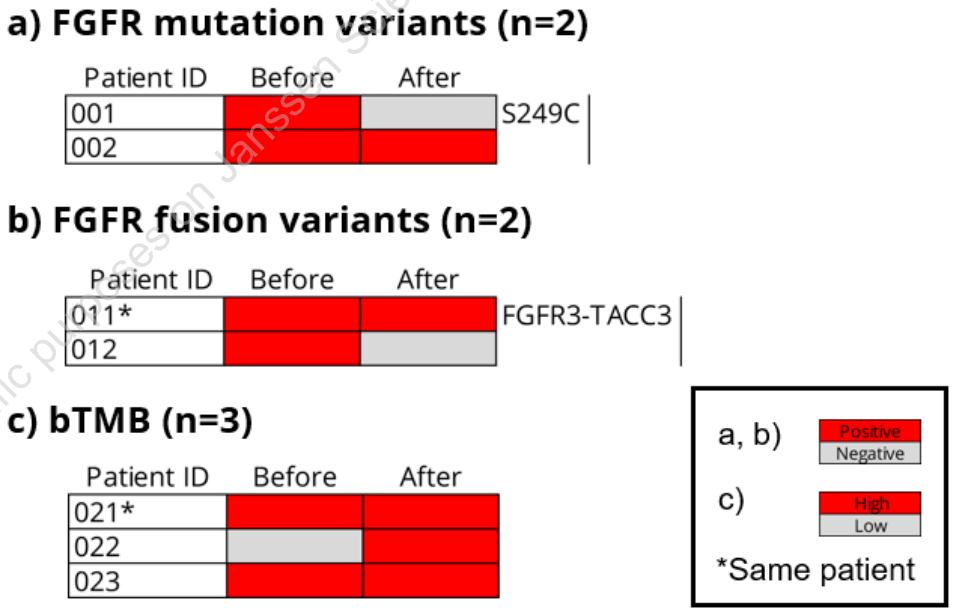


Figure 7: Sample-level concordance of gene mutation status; Before vs. after treatment



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3) Yohann Loriot et al. N Engl J Med. 2019 Jul 25;381(4): 338-349.

DISCLOSURES:

This study was conducted and founded by Janssen Pharmaceutical K.K., Japan. Janssen Pharmaceutical K.K. was one of the participating companies in the MONSTAR SCREEN database study. Nobuaki Matsubara has received consulting or advisory roles from Sanofi, Janssen, AstraZeneca, Lilly, Amgen, Seagen, Pfizer, honoraria from Sanofi, and research funding from Janssen, MSD, Bayer Yakuhin, Chugai Pharma, AstraZeneca, Astellas Pharma, Bayer, Amgen, Takeda, Lilly, Eisai, Roche/Genentech, Seagen, Novartis, and Abbvie. Takahiro Osawa has received honoraria from Takeda and Ono Pharma. Mototsugu Oya has received consulting or advisory roles from Bayer, and honoraria from Pfizer, Bayer, Ono Pharma, Bristol-Myers Squibb Japan, Astellas Pharma, Janssen, AstraZeneca, Takeda, MSD, Eisai, Merck, and research funding from Astellas Pharma. Toshiyuki Iwahori has received honoraria from Shiga University of medical science. Toshiyuki Iwahori, Hiroaki Tsuchiya, Maiko Murota, Masaki Yoshida, Yohei Tatematsu, and Yosuke Nakano are employees of Janssen. Masatoshi Eto has received consulting or advisory roles from Eisai, Pfizer, Takeda, Merck, MSD, Chugai Pharma, and speakers' bureau from MSD, Merck, AstraZeneca, Eisai, Ono Pharma, Takeda, Bristol-Myers Squibb, Astellas Pharma, Pfizer, Janssen, and research funding from Takeda. Norio Nonomura has received honoraria from Janssen, Takeda, Astellas Pharma, and patents, royalties, and other intellectual property from Shionogi. Takashige Abe and Koshiro Nishimoto have no conflict of interest to declare.

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