

Evolution of real-world treatment patterns over time in patients with *HER2*-negative advanced gastric cancer: a retrospective database cohort study from Japan

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Supplementary material

Supplementary Table S1 Insurance claims codes for diagnoses and medical procedures used in the database study

ICD-10 diagnosis code	Description
C16	Malignant neoplasm of stomach
C16.0	Malignant neoplasm: Cardia
C16.1	Malignant neoplasm: Fundus of stomach
C16.2	Malignant neoplasm: Body of stomach
C16.3	Malignant neoplasm: Pyloric antrum
C16.4	Malignant neoplasm: Pylorus
C16.5	Malignant neoplasm: Lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm: Greater curvature of stomach, unspecified
C16.8	Malignant neoplasm: Overlapping lesion of stomach
C16.9	Malignant neoplasm: Stomach, unspecified
Surgical procedure receipt code	Description
150168110	Total gastric resection (malignant tumor surgery) [K6572]
150168010	Gastric resection (malignant tumor surgery) [K6552]
150323510	Laparoscopic gastric local site resection (malignant tumor surgery) [K655-22]
150323710	Laparoscopic total gastric resection (malignant tumor surgery) [K657-22]
150337310	Proximal gastrectomy (malignant tumor resection) [K655-42]
150407110	Laparoscopic total gastric resection (malignant tumor surgery) (with supportive device for endoscopic surgery) [K657-22]
150377910	Laparoscopic proximal gastrectomy (malignant tumor resection) [K655-52]
150406910	Laparoscopic gastric partial resection (with malignant tumor resection/surgery support instrument) [K655-52]
150406710	Laparoscopic gastric local site resection (surgery for malignant tumor) (with supportive device for endoscopic surgery) [K655-22]

ICD-10 International Classification of Diseases, 10th revision

Supplementary Table S2 Insurance claims codes for Japanese Gastric Cancer Association guideline-recommended antitumor agents

Receipt code	Generic name	Description
620001919	Cisplatin	IA-call 100 mg for IA injection
620002591		IA-call 50 mg for IA injection
620004129		Cisplatin injection 10 mg/20 mL (NICHIIKO)
620004130		Cisplatin injection 25 mg/50 mL (NICHIIKO)
620004131		Cisplatin injection 50 mg/100 mL (NICHIIKO)
620006298		Briplatin injection 10 mg/20 mL
620006299		Briplatin injection 25 mg/50 mL
620006300		Briplatin injection 50 mg/100 mL
620008946		Randa injection 10 mg/20 mL
620008947		Randa injection 25 mg/50 mL
620008948		Randa injection 50 mg/100 mL
620009545		Cisplatin IV infusion 10 mg/20 mL (MYLAN)
620009546		Cisplatin IV infusion 25 mg/50 mL (MYLAN)
620009547		Cisplatin IV infusion 50 mg/100 mL (MYLAN)
620923202		Cisplatin IV infusion 10 mg/20 mL (PFIZER)
620923301		Cisplatin IV infusion 10 mg/20 mL (MARUKO)
620923602		Cisplatin IV infusion 25 mg/50 mL (PFIZER)
620923701		Cisplatin IV infusion 25 mg/50 mL (MARUKO)
620924002		Cisplatin IV infusion 50 mg/100 mL (PFIZER)
620924101		Cisplatin IV infusion 50 mg/100 mL (MARUKO)
622760800		Cisplatin IV infusion 10 mg/20 mL
622760900		Cisplatin IV infusion 25 mg/50 mL
622761000		Cisplatin IV infusion 50 mg/100 mL
640406088		Cisplatin injection 10 mg/20 mL (MARUKO)
640406089		Cisplatin injection 25 mg/50 mL (MARUKO)
640406090		Cisplatin injection 50 mg/100 mL (MARUKO)
644210052		Briplatin injection 50 mg/100 mL
644210053		Briplatin injection 25 mg/50 mL
644210054		Briplatin injection 10 mg/20 mL
644210055		Randa injection 50 mg/100 mL
644210056		Randa injection 25 mg/50 mL
644210057		Randa injection 10 mg/20 mL

644290002		Platosin injection 10 mg/20 mL
644290003		Platosin injection 25 mg/50 mL
644290004		Platosin injection 50 mg/100 mL
620002490	Oxaliplatin	Elplat for injection 100 mg
620008572		Elplat for injection 50 mg
621932201		Elplat IV infusion 50 mg/10 mL
621932301		Elplat IV infusion 100 mg/20 mL
622189401		Elplat IV infusion 200 mg/40 mL
622371101		Oxaliplatin IV infusion 50 mg/10 mL (DSEP)
622371201		Oxaliplatin IV infusion 100 mg/20 mL (DSEP)
622371801		Oxaliplatin IV infusion 50 mg/10 mL (TOWA)
622371901		Oxaliplatin IV infusion 100 mg/20 mL (TOWA)
622373201		Oxaliplatin IV infusion 50 mg/10 mL (FFP)
622373301		Oxaliplatin IV infusion 100 mg/20 mL (FFP)
622374801		Oxaliplatin IV infusion 50 mg/10 mL (HOSPIRA)
622374901		Oxaliplatin IV infusion 100 mg/20 mL (HOSPIRA)
622381301		Oxaliplatin IV infusion 50 mg/10 mL (PFIZER)
622381401		Oxaliplatin IV infusion 100 mg/20 mL (PFIZER)
622383201		Oxaliplatin IV infusion 50 mg/10 mL (SANDOZ)
622383301		Oxaliplatin IV infusion 100 mg/20 mL (SANDOZ)
622385701		Oxaliplatin IV infusion 50 mg/10 mL (NK)
622385801		Oxaliplatin IV infusion 100 mg/20 mL (NK)
622388601		Oxaliplatin IV infusion 50 mg/10 mL (CHEMIPHAR)
622388701		Oxaliplatin IV infusion 100 mg/20 mL (CHEMIPHAR)
622389801		Oxaliplatin IV infusion 50 mg/10 mL (SAWAI)
622389901		Oxaliplatin IV infusion 100 mg/20 mL (SAWAI)
622392001		Oxaliplatin IV infusion 50 mg/10 mL (NIPRO)
622392101		Oxaliplatin IV infusion 100 mg/20 mL (NIPRO)
622393201		Oxaliplatin IV infusion 50 mg/10 mL (NICHIIKO)
622393301		Oxaliplatin IV infusion 100 mg/20 mL (NICHIIKO)
622394701		Oxaliplatin IV infusion 50 mg/10 mL (TEVA)
622394801		Oxaliplatin IV infusion 100 mg/20 mL (TEVA)
622411901		Oxaliplatin IV infusion 200 mg/40 mL (TOWA)
622417801		Oxaliplatin IV infusion 200 mg/40 mL (PFIZER)
622426801		Oxaliplatin IV infusion 200 mg/40 mL (DSEP)
622428001		Oxaliplatin IV infusion 200 mg/40 mL (CHEMIPHAR)

622431101		Oxaliplatin IV infusion 200 mg/40 mL (SAWAI)
622432401		Oxaliplatin IV infusion 200 mg/40 mL (TEVA)
622434901		Oxaliplatin IV infusion 200 mg/40 mL (NK)
622437001		Oxaliplatin IV infusion 200 mg/40 mL (NICHIIKO)
622437201		Oxaliplatin IV infusion 50 mg/10 mL (KCC)
622437301		Oxaliplatin IV infusion 100 mg/20 mL (KCC)
622437401		Oxaliplatin IV infusion 200 mg/40 mL (KCC)
622439101		Oxaliplatin IV infusion 200 mg/40 mL (NIPRO)
622460601		Oxaliplatin IV infusion 200 mg/40 mL (HOSPIRA)
622461701		Oxaliplatin IV infusion 200 mg/40 mL (SANDOZ)
622476900		Oxaliplatin 100 mg/20 mL injection
622617800		Oxaliplatin 50 mg/10 mL injection
622617900		Oxaliplatin 200 mg/40 mL injection
610470009	Capecitabine	Xeloda tablets 300 mg
622656401		Capecitabine tablets 300 mg (SAWAI)
622674301		Capecitabine tablets 300 mg (NICHIIKO)
622677701		Capecitabine tablets 300 mg (TOWA)
622679001		Capecitabine tablets 300 mg (YAKULT)
622695801		Capecitabine tablets 300 mg (NK)
622700101		Capecitabine tablets 300 mg (JG)
620005087	Tegafur	Futraful enteric-coated granules 50%
620004748		Futraful injection 400 mg/10 mL
620004566		Futraful capsules 200 mg
620004820		Futraful suppositories 750 mg
621930101	Tegafur/uracil	UFT E combination granules 200 mg (equivalent tegafur)
620003181		UFT capsules (equivalent tegafur)
620915001		UFT combination capsules 100 mg (equivalent tegafur)
621929901		UFT E combination granules 100 mg (equivalent tegafur)
620004602		UFT E granules 20% (equivalent tegafur)
621930001		UFT E combination granules 150 mg (equivalent tegafur)
610421353	S-1	TS-1 capsules 20 mg (equivalent tegafur)
610421354		TS-1 capsules 25 mg (equivalent tegafur)
620009353		TS-1 combination granules 20 mg (equivalent tegafur)
620009354		TS-1 combination granules 25 mg (equivalent tegafur)
620915501		TS-1 combination capsules 20 mg (equivalent tegafur)
620915601		TS-1 combination capsules 25 mg (equivalent tegafur)

622243001		TS-1 combination OD tablets 20 mg (equivalent tegafur)
622243101		TS-1 combination OD tablets 25 mg (equivalent tegafur)
622254901		NKS-1 combination capsules 20 mg (equivalent tegafur)
622255001		NKS-1 combination capsules 25 mg (equivalent tegafur)
622256001		Esueewan combination capsules 20 mg (equivalent tegafur)
622256101		Esueewan combination capsules 25 mg (equivalent tegafur)
622275701		Temeral combination capsules 20 mg (equivalent tegafur)
622275801		Temeral combination capsules 25 mg (equivalent tegafur)
622285701		S-1Meiji combination capsules 20 mg (equivalent tegafur)
622294601		S-1 NP combination capsules 20 mg (equivalent tegafur)
622294701		S-1 NP combination capsules 25 mg (equivalent tegafur)
622397101		EES-1 combination tablets 20 mg (equivalent tegafur)
622397201		EES-1 combination tablets 25 mg (equivalent tegafur)
622397301		S-1KK combination tablets 20 mg (equivalent tegafur)
622397401		S-1KK combination tablets 25 mg (equivalent tegafur)
622430801		Esueewan combination granules 20 mg (equivalent tegafur)
622430901		Esueewan combination granules 25 mg (equivalent tegafur)
622434701		NKS-1 combination granules 20 mg (equivalent tegafur)
622434801		NKS-1 combination granules 25 mg (equivalent tegafur)
622487301		NKS-1 combination OD tablets 20 mg (equivalent tegafur)
622487401		NKS-1 combination OD tablets 25 mg (equivalent tegafur)
622497901		Esueewan combination OD tablets 20 mg (equivalent tegafur)
622498001		Esueewan combination OD tablets 25 mg (equivalent tegafur)
622537501		S-1TAIHO combination OD tablets 20 mg (equivalent tegafur)
622537601		S-1TAIHO combination OD tablets 25 mg (equivalent tegafur)
622285801		S-1Meiji combination capsules 25 mg (equivalent tegafur)
622047901	5-Fluorouracil	5-FU injection 1000 mg
622229101		5-FU injection 250 mg
622412501		Fluorouracil injection 250 mg (TOWA)
622412601		Fluorouracil injection 1000 mg (TOWA)
640463105		5-FU injection 250 mg KYOWA
622336001	Trifluridine/tipiracil	Lonsurf combination tablets 15 mg (equivalent trifluridine)
622336101		Lonsurf combination tablets 20 mg (equivalent trifluridine)
620003751	Paclitaxel	Taxol injection 30 mg/5 mL
620003752		Taxol injection 100 mg/16.7 mL
620004170		Paclitaxel injection 30 mg/5 mL (NK)

620004171		Paclitaxel injection 100 mg/16.7 mL (NK)
620005688		Paclitaxel injection 30 mg/5 mL (SAWAI)
620005689		Paclitaxel injection 100 mg/16.7 mL (SAWAI)
620005690		Paclitaxel injection 150 mg/25 mL (SAWAI)
622009101		Paclitaxel injection 30 mg/5 mL (MYLAN)
622009102		Paclitaxel injection 30 mg/5 mL (PFIZER)
622009201		Paclitaxel injection 100 mg/16.7 mL (MYLAN)
622009202		Paclitaxel injection 100 mg/16.7 mL (PFIZER)
622082001		Paclitaxel IV infusion 30 mg/5 mL (SANDOZ)
622082101		Paclitaxel IV infusion 100 mg/16.7 mL (SANDOZ)
622259101		Paclitaxel injection 30 mg/5 mL (NP)
622259201		Paclitaxel injection 100 mg 16.7 mL (NP)
622375001		Paclitaxel IV infusion 30 mg/5 mL (HOSPIRA)
622375101		Paclitaxel IV infusion 100 mg/16.7 mL (HOSPIRA)
622760500		Paclitaxel IV infusion 30 mg/5 mL
622760600		Paclitaxel IV infusion 100 mg/16.7 mL
622760700		Paclitaxel IV infusion 150 mg/25 mL
621970101	nab-Paclitaxel	Abraxane for IV infusion 100 mg
620007257	Irinotecan	Campto IV infusion 40 mg/2 mL
620007258		Campto IV infusion 100 mg/5 mL
620009515		Irinotecan hydrochloride IV infusion 40 mg/2 mL (NK)
620009516		Irinotecan hydrochloride IV infusion 40 mg/2 mL (SAWAI)
620009517		Irinotecan hydrochloride IV infusion 40 mg/2 mL (SANDOZ)
620009518		Irinotecan hydrochloride IV infusion 40 mg/2 mL (TAIHO)
620009519		Irinotecan hydrochloride IV infusion 100 mg/5 mL (NK)
620009520		Irinotecan hydrochloride IV infusion 100 mg/5 mL (SAWAI)
620009521		Irinotecan hydrochloride IV infusion 100 mg/5 mL (SANDOZ)
620009522		Irinotecan hydrochloride IV infusion 100 mg/5 mL (TAIHO)
620919501		Topotecin IV infusion 40 mg/2 mL
620919701		Topotecin IV infusion 100 mg/5 mL
621900302		Irinotecan hydrochloride IV infusion 40 mg/2 mL (SUN)
621900402		Irinotecan hydrochloride IV infusion 100 mg/5 mL (SUN)
622019401		Irinotecan hydrochloride IV infusion 40 mg/2 mL (HOSPIRA)
622019501		Irinotecan hydrochloride IV infusion 100 mg/5 mL (HOSPIRA)
622059701		Irinotecan hydrochloride IV infusion 40 mg/2 mL (TAIYO)
622059801		Irinotecan hydrochloride IV infusion 100 mg/5 mL (TAIYO)

622091101		Irinotecan hydrochloride IV infusion 40 mg/2 mL (ASKA)
622091201		Irinotecan hydrochloride IV infusion 100 mg/5 mL (ASKA)
622230201		Irinotecan hydrochloride IV infusion 40 mg/2 mL (NICHIIKO)
622230301		Irinotecan hydrochloride IV infusion 100 mg/5 mL (NICHIIKO)
622236901		Irinotecan hydrochloride IV infusion 40 mg/2 mL (TOWA)
622237001		Irinotecan hydrochloride IV infusion 100 mg/5 mL (TOWA)
622470401		Irinotecan hydrochloride IV infusion 40 mg/2 mL (HENGROI)
622470501		Irinotecan hydrochloride IV infusion 100 mg/5 mL (HENGROI)
622258901		Irinotecan hydrochloride IV infusion 40 mg/2 mL (NP)
622259001		Irinotecan hydrochloride IV infusion 100 mg/5 mL (NP)
644290006		Campto injection 40 mg/2 mL
644290007		Campto injection 100 mg/5 mL
644290008		Topotecin injection 40 mg/2 mL
644290009		Topotecin injection 100 mg/5 mL
620919801	Docetaxel	Taxotere for IV infusion 20 mg/0.5 mL (w/solution)
620919901		Taxotere for IV infusion 80 mg/2 mL (w/solution)
622068501		Onetaxotere IV infusion 20 mg/1mL
622068601		Onetaxotere IV infusion 80 mg/4mL
622215301		Docetaxel IV infusion 20 mg/2 mL (SANDOZ)
622215401		Docetaxel IV infusion 80 mg/8mL (SANDOZ)
622231801		Docetaxel for IV infusion 20 mg/0.5 mL(w/solution) (ASKA)
622231901		Docetaxel for IV infusion 80 mg/2 mL(w/solution) (ASKA)
622272001		Docetaxel IV infusion 20 mg/1mL (TOWA)
622272101		Docetaxel IV infusion 80 mg/4mL (TOWA)
622283101		Docetaxel IV infusion 20 mg/1mL (TEVA)
622283201		Docetaxel IV infusion 80 mg/4mL (TEVA)
622285201		Docetaxel IV infusion 20 mg/2 mL (HOSPIRA)
622285301		Docetaxel IV infusion 80 mg/8mL (HOSPIRA)
622285401		Docetaxel IV infusion 120 mg/12 mL (HOSPIRA)
622290401		Docetaxel IV infusion 20 mg/1mL (HK)
622290501		Docetaxel IV infusion 80 mg/4mL (HK)
622294901		Docetaxel IV infusion 20 mg/1mL (CHEMIPHAR)
622295001		Docetaxel IV infusion 80 mg/4mL (CHEMIPHAR)
622295501		Docetaxel for IV infusion 20 mg/0.5 mL (w/solution) (SAWAI)
622295601		Docetaxel for IV infusion 80 mg/2 mL (w/solution) (SAWAI)
622354801		Docetaxel IV infusion 20 mg/1mL (NK)

622354901		Docetaxel IV infusion 80 mg/4mL (NK)
622356401		Docetaxel IV infusion 20 mg/1mL (SAWAI)
622356501		Docetaxel IV infusion 80 mg/4mL (SAWAI)
622408501		Docetaxel IV infusion 20 mg/1mL (YAKULT)
622408601		Docetaxel IV infusion 80 mg/4mL (YAKULT)
622417601		Docetaxel IV infusion 20 mg/1mL (PFIZER)
622417701		Docetaxel IV infusion 80 mg/4mL (PFIZER)
622429301		Docetaxel IV infusion 20 mg/1mL (EE)
622429401		Docetaxel IV infusion 80 mg/4mL (EE)
622435002		Docetaxel IV infusion 20 mg/1mL (NIPRO)
622435102		Docetaxel IV infusion 80 mg/4mL (NIPRO)
640411025		Taxotere injection 20 mg/0.5 mL (w/solution)
640411026		Taxotere injection 80 mg/2 mL (w/solution)
620001938	Trastuzumab	Herceptin for injection 60 mg (w/solution, dilution)
622069801		Herceptin for injection 60 mg (w/solution)
622069901		Herceptin for injection 150 mg (w/solution)
622630701		Trastuzumab BS for IV infusion 60 mg (NK)
622630801		Trastuzumab BS for IV infusion 150 mg (NK)
622659701		Trastuzumab BS for IV infusion 60 mg (DAIICHI-SANKYO) (w/solution)
622659801		Trastuzumab BS for IV infusion 150 mg (DAIICHI-SANKYO) (w/solution)
622679201		Trastuzumab BS for IV infusion 60 mg (PFIZER)
622679301		Trastuzumab BS for IV infusion 150 mg (PFIZER)
640451013		Herceptin for injection 150 mg (w/solution, dilution)
622628901		Trastuzumab BS for IV infusion 60 mg (CTH)
622629001		Trastuzumab BS for IV infusion 150 mg (CTH)
629907101	Trastuzumab deruxtecan	Enhertu for IV infusion 100 mg
622417901	Ramucirumab	Cyramza IV infusion 100 mg/10 mL
622418001		Cyramza IV infusion 500 mg/50 mL
622364801	Nivolumab	Opdivo IV infusion 20 mg/2 mL
622364901		Opdivo IV infusion 100 mg/10 mL
622662201		Opdivo IV infusion 240 mg/24mL
629911501		Opdivo IV infusion 120 mg/12 mL
622515701	Pembrolizumab	Keytruda IV infusion 20 mg/0.8mL
622515801		Keytruda IV infusion 100 mg/4mL

620005715	Levofolinate calcium	Revo folinate IV infusion 25 mg (OHARA)
620005716		Revo folinate IV infusion 25 mg (HK)
620005717		Revo folinate IV infusion 25 mg (NK)
620005718		Revo folinate IV infusion 25 mg (NP)
620005719		Revo folinate IV infusion 25 mg (F)
620005720		Revo folinate IV infusion 25 mg (SAWAI)
620005721		Revo folinate IV infusion 25 mg (TAIYO)
620005722		Revo folinate IV infusion 25 mg (TOWA)
620005723		Revo folinate IV infusion 25 mg (NICHIIKO)
620005724		Revo folinate IV infusion 25 mg (BT)
620005725		Revo folinate IV infusion 25 mg (YAKULT)
620005726		Revo folinate IV infusion 50 mg (NICHIIKO)
620005727		Revo folinate IV infusion 100 mg (OHARA)
620005728		Revo folinate IV infusion 100 mg (NK)
620005729		Revo folinate IV infusion 100 mg (TOWA)
620005730		Revo folinate IV infusion 100 mg (YAKULT)
620005879		Revo folinate IV infusion 100 mg (HK)
620005880		Revo folinate IV infusion 100 mg (NP)
620005881		Revo folinate IV infusion 100 mg (SAWAI)
620008234		Revo folinate IV infusion 100 mg (F)
620008543		Revo folinate IV infusion 100 mg (NICHIIKO)
620009589		Revo folinate IV infusion 100 mg (TAIYO)
620009590		Revo folinate IV infusion 100 mg (BT)
622693500		Revo folinate calcium for injection 25 mg
622758000		Revo folinate calcium for injection 100 mg
622758100		Revo folinate calcium for injection 50 mg
629930301	Zolbetuximab	Vyloy for injection 100 mg

5-FU 5-fluorouracil, BCG Bacillus Calmette–Guérin, BS biosimilar, IA intra-arterial, ICD-10 International Classification of Diseases 10th revision, IV intravenous, OD once daily, S-1 tegafur/gimeracil/oteracil potassium, SC subcutaneous, w/ with

Supplementary Table S3 Study objectives

Primary objective
Describe treatment patterns in patients with aGC by era and regimen, with a particular focus on combination therapy with Nivo + CT or other CT as 1L therapy, based on the following: - Proportion of patients receiving each regimen in first-, second-, and third-line treatment - Sequence of 1L to 3L treatment - DoT of each line - Overall DoT from 1L to last line - Transition rate from 1L to 2L and from 2L to 3L
Secondary objective
In patients who received 1L treatment with Nivo + CT vs other CT, describe DoT, transition rates, and treatment patterns
<i>1L</i> first-line, <i>2L</i> second-line, <i>3L</i> third-line, <i>aGC</i> advanced gastric cancer, <i>CT</i> chemotherapy, <i>DoT</i> duration of therapy, <i>Nivo</i> nivolumab

Supplementary Table S4 Treatment regimens included only those recommended by the 2021 Japanese Gastric Cancer Association guidelines for *HER2*-negative advanced gastric cancer [1]

Recommended regimens	Conditionally recommended regimens
S-1 + CDDP	5-FU + CDDP
Cape + CDDP	5-FU + I-LV
SOX	5-FU + I-LV + PTX
CapeOX	S-1
FOLFOX	S-1 + DTX
Nivo + SOX	
Nivo + CapeOX	
Nivo + FOLFOX	

5-FU fluorouracil, *Cape* capecitabine, *CapeOX* capecitabine plus oxaliplatin, *CDDP* cis-diamminedichloroplatinum (cisplatin), *DTX* docetaxel, *FOLFOX* folinic acid + fluorouracil plus oxaliplatin, *I-LV* levoleucovorin, *Nivo* nivolumab, *PTX* paclitaxel, *S-1* tegafur + gimeracil + oteracil, *SOX* S-1 plus oxaliplatin

Supplementary Table S5 Definitions related to treatment and study outcomes

Treatment definition	Description
Regimen in each LoT	Any combination regimen listed in the JGCA guideline [1] that was prescribed within 35 days after the start of the treatment
Start of regimen	The first date with a record of administration of any agents in the regimen
End of LoT	A different agent not in the prior LoT regimen was started within 120 days after the last administration of agents in the prior regimen, or when all antitumor agents in the regimen were not prescribed for 120 days For oral agents, the last administration date was estimated based on the date of the last prescription plus the number of days' supply
Study outcome	Description
Patient characteristics	Extracted for each cohort based on the start date of 1L treatment
Designated cancer care hospital	Medical institutions accredited by the Japanese Ministry of Health, Labour and Welfare to standardize cancer care, centralize patients, and improve clinical outcomes through multidisciplinary and high-quality cancer treatment"
Hospital information (i.e., number of beds, type of hospital)	Extracted for each cohort based on the start date of 1L treatment
Selected comorbidities	Collected for the 180-day period before the start of 1L treatment for each cohort
Metastasis sites	Collected for the 180-day period before the start of 1L treatment for each cohort
10-item Barthel ADL index score [2]	Extracted to assess functional independence; scores were defined as "independent" if all 10 items were reported as independent and "dependent" if any of the 10 items were reported as dependent
Follow-up	Collected from the discharge summary of the last hospitalization that occurred within 180 days prior to the start of 1L treatment

1L first-line, ADL Activities of Daily Living, JGCA Japanese Gastric Cancer Association, LoT line of treatment

Supplementary Table S6 Insurance claims codes for Cox regression analysis of alpha-fetoprotein testing

Kubun code	Receipt code	Description
D009	160036010	AFP [D0091]
D009	160036710	AFP [D0093]

AFP alpha-fetoprotein

Supplementary Table S7 Patient baseline characteristics by age category (<75 vs ≥75 years)

Characteristic ^a	<75 years							≥75 years						
	Overall	Era 1	Era 2	Era 3	Era 4	Era 5	Era 6	Overall	Era 1	Era 2	Era 3	Era 4	Era 5	Era 6
	N=11,697	(2012– 2013) N=630	(2014– 2015) N=1,305	(2016– 2017) N=2,001	(2018– 2019) N=2,559	(2020– 2021) N=2,608	(2022– 2023) N=2,594	N=4,876	(2012– 2013) N=152	(2014– 2015) N=339	(2016– 2017) N=612	(2018– 2019) N=1,080	(2020– 2021) N=1,188	(2022– 2023) N=1,505
Sex														
Male	8,393 (71.8)	451 (71.6)	916 (70.2)	1,455 (72.7)	1,833 (71.6)	1,884 (72.2)	1,854 (71.5)	3,562 (73.1)	118 (77.6)	245 (72.3)	445 (72.7)	783 (72.5)	886 (74.6)	1,085 (72.1)
Female	3,304 (28.2)	179 (28.4)	389 (29.8)	546 (27.3)	726 (28.4)	724 (27.8)	740 (28.5)	1,314 (26.9)	34 (22.4)	94 (27.7)	167 (27.3)	297 (27.5)	302 (25.4)	420 (27.9)
Number of beds in hospital														
<200	549 (4.7)	31 (4.9)	62 (4.8)	86 (4.3)	131 (5.1)	120 (4.6)	119 (4.6)	253 (5.2)	11 (7.2)	22 (6.5)	39 (6.4)	46 (4.3)	56 (4.7)	79 (5.2)
200–499	6,067 (51.9)	403 (64.0)	694 (53.2)	1,046 (52.3)	1,276 (49.9)	1,350 (51.8)	1,298 (50.0)	2,639 (54.1)	92 (60.5)	187 (55.2)	336 (54.9)	575 (53.2)	648 (54.5)	801 (53.2)
≥500	5,081 (43.4)	196 (31.1)	549 (42.1)	869 (43.4)	1,152 (45.0)	1,138 (43.6)	1,177 (45.4)	1,984 (40.7)	49 (32.2)	130 (38.3)	237 (38.7)	459 (42.5)	484 (40.7)	625 (41.5)
Designated cancer hospital ^b														
Yes	9,714 (83.0)	492 (78.1)	1,075 (82.4)	1,652 (82.6)	2,160 (84.4)	2,148 (82.4)	2,187 (84.3)	3,915 (80.3)	106 (69.7)	276 (81.4)	469 (76.6)	886 (82.0)	956 (80.5)	1,222 (81.2)
No	1,983 (17.0)	138 (21.9)	230 (17.6)	349 (17.4)	399 (15.6)	460 (17.6)	407 (15.7)	961 (19.7)	46 (30.3)	63 (18.6)	143 (23.4)	194 (18.0)	232 (19.5)	283 (18.8)
Age, median (range), years	67 (20, 74)	65 (22, 74)	66 (20, 74)	67 (26, 74)	67 (21, 74)	68 (21, 74)	68 (22, 74)	78 (75, 93)	78 (75, 86)	77 (75, 90)	78 (75, 89)	78 (75, 91)	78 (75, 91)	78 (75, 93)
Metastasis site														
Peritoneal or ascites	3,138 (26.8)	159 (25.2)	349 (26.7)	528 (26.4)	704 (27.5)	726 (27.8)	672 (25.9)	955 (19.6)	29 (19.1)	54 (15.9)	123 (20.1)	218 (20.2)	241 (20.3)	290 (19.3)
Liver	2,144 (18.3)	156 (24.8)	271 (20.8)	376 (18.8)	444 (17.4)	480 (18.4)	417 (16.1)	1,049 (21.5)	37 (24.3)	88 (26.0)	160 (26.1)	239 (22.1)	253 (21.3)	272 (18.1)
Lymph node	1,996 (17.1)	141 (22.4)	261 (20.0)	354 (17.7)	410 (16.0)	427 (16.4)	403 (15.5)	794 (16.3)	29 (19.1)	64 (18.9)	94 (15.4)	175 (16.2)	205 (17.3)	227 (15.1)
Lung	390 (3.3)	24 (3.8)	44 (3.4)	78 (3.9)	86 (3.4)	73 (2.8)	85 (3.3)	191 (3.9)	10 (6.6)	13 (3.8)	22 (3.6)	38 (3.5)	56 (4.7)	52 (3.5)
Bone	520 (4.4)	34 (5.4)	54 (4.1)	86 (4.3)	118 (4.6)	109 (4.2)	119 (4.6)	133 (2.7)	3 (2.0)	12 (3.5)	17 (2.8)	27 (2.5)	39 (3.3)	35 (2.3)
Brain	48 (0.4)	2 (0.3)	4 (0.3)	10 (0.5)	13 (0.5)	10 (0.4)	9 (0.3)	16 (0.3)	0	0	1 (0.2)	8 (0.7)	5 (0.4)	2 (0.1)
Comorbidities														
Hypertension	2,761 (23.6)	140 (22.2)	289 (22.1)	407 (20.3)	634 (24.8)	644 (24.7)	647 (24.9)	1,643 (33.7)	45 (29.6)	97 (28.6)	216 (35.3)	376 (34.8)	388 (32.7)	521 (34.6)
Edema	255 (2.2)	15 (2.4)	29 (2.2)	40 (2.0)	60 (2.3)	54 (2.1)	57 (2.2)	121 (2.5)	4 (2.6)	4 (1.2)	15 (2.5)	40 (3.7)	18 (1.5)	40 (2.7)

Liver diseases	1,668 (14.3)	46 (7.3)	154 (11.8)	279 (13.9)	384 (15.0)	375 (14.4)	430 (16.6)	707 (14.5)	13 (8.6)	39 (11.5)	84 (13.7)	171 (15.8)	157 (13.2)	243 (16.1)
Renal disease	782 (6.7)	40 (6.3)	76 (5.8)	132 (6.6)	163 (6.4)	185 (7.1)	186 (7.2)	337 (6.9)	3 (2.0)	17 (5.0)	41 (6.7)	69 (6.4)	87 (7.3)	120 (8.0)
Diabetes	2,384 (20.4)	109 (17.3)	254 (19.5)	381 (19.0)	503 (19.7)	535 (20.5)	602 (23.2)	1,186 (24.3)	36 (23.7)	71 (20.9)	134 (21.9)	272 (25.2)	265 (22.3)	408 (27.1)
Thrombosis	863 (7.4)	30 (4.8)	82 (6.3)	135 (6.7)	213 (8.3)	176 (6.7)	227 (8.8)	427 (8.8)	6 (3.9)	23 (6.8)	48 (7.8)	99 (9.2)	103 (8.7)	148 (9.8)
Ischemic heart disease	586 (5.0)	24 (3.8)	58 (4.4)	100 (5.0)	144 (5.6)	116 (4.4)	144 (5.6)	419 (8.6)	18 (11.8)	23 (6.8)	60 (9.8)	88 (8.1)	88 (7.4)	142 (9.4)
Hemorrhoids	173 (1.5)	7 (1.1)	21 (1.6)	29 (1.4)	42 (1.6)	44 (1.7)	30 (1.2)	67 (1.4)	0	6 (1.8)	8 (1.3)	18 (1.7)	16 (1.3)	19 (1.3)
Neuropathy	349 (3.0)	16 (2.5)	29 (2.2)	61 (3.0)	86 (3.4)	73 (2.8)	84 (3.2)	165 (3.4)	1 (0.7)	3 (0.9)	23 (3.8)	50 (4.6)	33 (2.8)	55 (3.7)
CCI score														
0	69 (0.6)	1 (0.2)	16 (1.2)	11 (0.5)	12 (0.5)	16 (0.6)	13 (0.5)	50 (1.0)	1 (0.7)	4 (1.2)	7 (1.1)	12 (1.1)	10 (0.8)	16 (1.1)
1	3 (0.0)	0	0	0	0	1 (0.0)	2 (0.1)	2 (0.0)	0	0	0	0	0	2 (0.1)
2	4,470 (38.2)	220 (34.9)	480 (36.8)	747 (37.3)	1,005 (39.3)	993 (38.1)	1,025 (39.5)	1,809 (37.1)	61 (40.1)	127 (37.5)	212 (34.6)	395 (36.6)	447 (37.6)	567 (37.7)
3	277 (2.4)	11 (1.7)	28 (2.1)	56 (2.8)	56 (2.2)	62 (2.4)	64 (2.5)	146 (3.0)	2 (1.3)	7 (2.1)	15 (2.5)	31 (2.9)	38 (3.2)	53 (3.5)
≥4	6,878 (58.8)	398 (63.2)	781 (59.8)	1,187 (59.3)	1,486 (58.1)	1,536 (58.9)	1,490 (57.4)	2,869 (58.8)	88 (57.9)	201 (59.3)	378 (61.8)	642 (59.4)	693 (58.3)	867 (57.6)
BMI category, kg/m ²														
<18.5	1,833 (20.9)	93 (21.4)	192 (20.8)	311 (21.0)	424 (21.6)	391 (19.5)	422 (21.3)	630 (17.0)	24 (21.1)	39 (16.7)	70 (14.9)	145 (17.7)	162 (17.7)	190 (16.4)
18.5–24.9	5,659 (64.4)	293 (67.5)	607 (65.6)	972 (65.7)	1,252 (63.9)	1,287 (64.2)	1,248 (63.0)	2,569 (69.2)	75 (65.8)	167 (71.4)	317 (67.4)	551 (67.3)	641 (70.1)	818 (70.6)
25–29.9	1,124 (12.8)	43 (9.9)	112 (12.1)	178 (12.0)	245 (12.5)	276 (13.8)	270 (13.6)	468 (12.6)	12 (10.5)	26 (11.1)	74 (15.7)	114 (13.9)	104 (11.4)	138 (11.9)
≥30	166 (1.9)	5 (1.2)	14 (1.5)	19 (1.3)	38 (1.9)	50 (2.5)	40 (2.0)	43 (1.2)	3 (2.6)	2 (0.9)	9 (1.9)	9 (1.1)	7 (0.8)	13 (1.1)
Missing	2,915	196	380	521	600	604	614	1,166	38	105	142	261	274	346

^aData are presented as n (%), unless otherwise stated; ^bDesignated cancer hospitals refers to a medical institution designated by Japan's Ministry of Health, Labour and Welfare to serve as a central facility for cancer treatment in Japan

BMI body mass index, *CCI* Charlson Comorbidity Index, *SD* standard deviation

Supplementary Table S8 Patient baseline characteristics by treatment facility (designated cancer hospital vs non-designated cancer hospital)

Characteristic ^a	Designated cancer hospital ^b							Non-designated cancer hospital ^b						
	Overall N=13,629	Era 1 (2012–2013) n=598	Era 2 (2014–2015) n=1,351	Era 3 (2016–2017) n=2,121	Era 4 (2018–2019) n=3,046	Era 5 (2021–2021) n=3,104	Era 6 (2022–2023) n=3,409	Overall N=2,944	Era 1 (2012–2013) n=184	Era 2 (2014–2015) n=293	Era 3 (2016–2017) n=492	Era 4 (2018–2019) n=593	Era 5 (2020–2021) n=692	Era 6 (2022–2023) n=690
Sex														
Male	9,735 (71.4)	430 (71.9)	950 (70.3)	1,525 (71.9)	2,178 (71.5)	2,245 (72.3)	2,407 (70.6)	2,220 (75.4)	139 (75.5)	211 (72.0)	375 (76.2)	438 (73.9)	525 (75.9)	532 (77.1)
Female	3,894 (28.6)	168 (28.1)	401 (29.7)	596 (28.1)	868 (28.5)	859 (27.7)	1,002 (29.4)	724 (24.6)	45 (24.5)	82 (28.0)	117 (23.8)	155 (26.1)	167 (24.1)	158 (22.9)
Number of beds in hospital														
<200	221 (1.6)	12 (2.0)	36 (2.7)	25 (1.2)	53 (1.7)	42 (1.4)	53 (1.6)	581 (19.7)	30 (16.3)	48 (16.4)	100 (20.3)	124 (20.9)	134 (19.4)	145 (21.0)
200–499	6,367 (46.7)	343 (57.4)	643 (47.6)	994 (46.9)	1,386 (45.5)	1,445 (46.6)	1,556 (45.6)	2,339 (79.4)	152 (82.6)	238 (81.2)	388 (78.9)	465 (78.4)	553 (79.9)	543 (78.7)
≥500	7,041 (51.7)	243 (40.6)	672 (49.7)	1,102 (52.0)	1,607 (52.8)	1,617 (52.1)	1,800 (52.8)	24 (0.8)	2 (1.1)	7 (2.4)	4 (0.8)	4 (0.7)	5 (0.7)	2 (0.3)
Age, median (range), years	70 (20, 92)	68 (22, 85)	68 (20, 88)	69 (26, 88)	70 (21, 89)	71 (21, 91)	72 (22, 92)	71 (26, 93)	70 (30, 86)	69 (27, 90)	70 (26, 89)	70 (39, 91)	72 (33, 90)	73 (30, 93)
Age category, years														
<65	3,657 (26.8)	231 (38.6)	453 (33.5)	629 (29.7)	828 (27.2)	769 (24.8)	747 (21.9)	623 (21.2)	52 (28.3)	87 (29.7)	110 (22.4)	126 (21.2)	133 (19.2)	115 (16.7)
65–74	6,057 (44.4)	261 (43.6)	622 (46.0)	1,023 (48.2)	1,332 (43.7)	1,379 (44.4)	1,440 (42.2)	1,360 (46.2)	86 (46.7)	143 (48.8)	239 (48.6)	273 (46.0)	327 (47.3)	292 (42.3)
≥75	3,915 (28.7)	106 (17.7)	276 (20.4)	469 (22.1)	886 (29.1)	956 (30.8)	1,222 (35.8)	961 (32.6)	46 (25.0)	63 (21.5)	143 (29.1)	194 (32.7)	232 (33.5)	283 (41.0)
Metastasis site														
Peritoneal or ascites	3,312 (24.3)	135 (22.6)	325 (24.1)	520 (24.5)	767 (25.2)	768 (24.7)	797 (23.4)	781 (26.5)	53 (28.8)	78 (26.6)	131 (26.6)	155 (26.1)	199 (28.8)	165 (23.9)
Liver	2,499 (18.3)	143 (23.9)	285 (21.1)	412 (19.4)	547 (18.0)	577 (18.6)	535 (15.7)	694 (23.6)	50 (27.2)	74 (25.3)	124 (25.2)	136 (22.9)	156 (22.5)	154 (22.3)
Lymph node	2,185 (16.0)	128 (21.4)	265 (19.6)	355 (16.7)	455 (14.9)	482 (15.5)	500 (14.7)	605 (20.6)	42 (22.8)	60 (20.5)	93 (18.9)	130 (21.9)	150 (21.7)	130 (18.8)
Lung	464 (3.4)	29 (4.8)	44 (3.3)	76 (3.6)	102 (3.3)	107 (3.4)	106 (3.1)	117 (4.0)	5 (2.7)	13 (4.4)	24 (4.9)	22 (3.7)	22 (3.2)	31 (4.5)
Bone	568 (4.2)	31 (5.2)	52 (3.8)	87 (4.1)	127 (4.2)	132 (4.3)	139 (4.1)	85 (2.9)	6 (3.3)	14 (4.8)	16 (3.3)	18 (3.0)	16 (2.3)	15 (2.2)
Brain	57 (0.4)	2 (0.3)	4 (0.3)	10 (0.5)	19 (0.6)	11 (0.4)	11 (0.3)	7 (0.2)	0	0	1 (0.2)	2 (0.3)	4 (0.6)	0
Comorbidities														
Hypertension	3,586 (26.3)	132 (22.1)	305 (22.6)	502 (23.7)	847 (27.8)	827 (26.6)	973 (28.5)	818 (27.8)	53 (28.8)	81 (27.6)	121 (24.6)	163 (27.5)	205 (29.6)	195 (28.3)
Edema	295 (2.2)	14 (2.3)	25 (1.9)	43 (2.0)	81 (2.7)	56 (1.8)	76 (2.2)	81 (2.8)	5 (2.7)	8 (2.7)	12 (2.4)	19 (3.2)	16 (2.3)	21 (3.0)
Liver diseases	2,039 (15.0)	40 (6.7)	162 (12.0)	303 (14.3)	476 (15.6)	465 (15.0)	593 (17.4)	336 (11.4)	19 (10.3)	31 (10.6)	60 (12.2)	79 (13.3)	67 (9.7)	80 (11.6)
Renal disease	912 (6.7)	33 (5.5)	74 (5.5)	138 (6.5)	188 (6.2)	215 (6.9)	264 (7.7)	207 (7.0)	10 (5.4)	19 (6.5)	35 (7.1)	44 (7.4)	57 (8.2)	42 (6.1)

Diabetes	3,003 (22.0)	116 (19.4)	286 (21.2)	422 (19.9)	664 (21.8)	662 (21.3)	853 (25.0)	567 (19.3)	29 (15.8)	39 (13.3)	93 (18.9)	111 (18.7)	138 (19.9)	157 (22.8)
Thrombosis	1,132 (8.3)	27 (4.5)	93 (6.9)	158 (7.4)	281 (9.2)	237 (7.6)	336 (9.9)	158 (5.4)	9 (4.9)	12 (4.1)	25 (5.1)	31 (5.2)	42 (6.1)	39 (5.7)
Ischemic heart disease	850 (6.2)	28 (4.7)	72 (5.3)	132 (6.2)	198 (6.5)	171 (5.5)	249 (7.3)	155 (5.3)	14 (7.6)	9 (3.1)	28 (5.7)	34 (5.7)	33 (4.8)	37 (5.4)
Hemorrhoids	188 (1.4)	4 (0.7)	20 (1.5)	29 (1.4)	49 (1.6)	50 (1.6)	36 (1.1)	52 (1.8)	3 (1.6)	7 (2.4)	8 (1.6)	11 (1.9)	10 (1.4)	13 (1.9)
Neuropathy	415 (3.0)	14 (2.3)	25 (1.9)	67 (3.2)	113 (3.7)	84 (2.7)	112 (3.3)	99 (3.4)	3 (1.6)	7 (2.4)	17 (3.5)	23 (3.9)	22 (3.2)	27 (3.9)
CCI score														
0	102 (0.7)	1 (0.2)	16 (1.2)	17 (0.8)	21 (0.7)	23 (0.7)	24 (0.7)	17 (0.6)	1 (0.5)	4 (1.4)	1 (0.2)	3 (0.5)	3 (0.4)	5 (0.7)
1	4 (0.0)	0	0	0	0	1 (0.0)	3 (0.1)	1 (0.0)	0	0	0	0	0	1 (0.1)
2	5,321 (39.0)	233 (39.0)	508 (37.6)	801 (37.8)	1,203 (39.5)	1,223 (39.4)	1,353 (39.7)	958 (32.5)	48 (26.1)	99 (33.8)	158 (32.1)	197 (33.2)	217 (31.4)	239 (34.6)
3	351 (2.6)	8 (1.3)	31 (2.3)	58 (2.7)	74 (2.4)	83 (2.7)	97 (2.8)	72 (2.4)	5 (2.7)	4 (1.4)	13 (2.6)	13 (2.2)	17 (2.5)	20 (2.9)
≥4	7,851 (57.6)	356 (59.5)	796 (58.9)	1,245 (58.7)	1,748 (57.4)	1,774 (57.2)	1,932 (56.7)	1,896 (64.4)	130 (70.7)	186 (63.5)	320 (65.0)	380 (64.1)	455 (65.8)	425 (61.6)
BMI category, kg/m ²														
<18.5	2,001 (19.5)	78 (19.4)	189 (20.0)	316 (19.9)	464 (19.9)	457 (19.3)	497 (19.0)	462 (20.6)	39 (26.9)	42 (19.6)	65 (17.9)	105 (23.6)	96 (17.3)	115 (22.2)
18.5–24.9	6,738 (65.7)	277 (68.7)	628 (66.5)	1,031 (65.0)	1,519 (65.1)	1,551 (65.6)	1,732 (66.1)	1,490 (66.5)	91 (62.8)	146 (68.2)	258 (70.9)	284 (63.8)	377 (68.1)	334 (64.4)
25–29.9	1,340 (13.1)	42 (10.4)	116 (12.3)	216 (13.6)	313 (13.4)	311 (13.2)	342 (13.1)	252 (11.2)	13 (9.0)	22 (10.3)	36 (9.9)	46 (10.3)	69 (12.5)	66 (12.7)
≥30	172 (1.7)	6 (1.5)	12 (1.3)	23 (1.5)	37 (1.6)	45 (1.9)	49 (1.9)	37 (1.7)	2 (1.4)	4 (1.9)	5 (1.4)	10 (2.2)	12 (2.2)	4 (0.8)
Missing	3,378	195	406	535	713	740	789	703	39	79	128	148	138	171

^aData are presented as n (%), unless otherwise stated; ^bDesignated cancer hospitals refers to a medical institution designated by Japan's Ministry of Health, Labour and Welfare to serve as a central facility for cancer treatment in Japan

BMI body mass index, *CCI* Charlson Comorbidity Index, *SD* standard deviation

Supplementary Table S9 Baseline characteristics in patients receiving chemotherapy alone or in combination with nivolumab in Eras 5 and 6

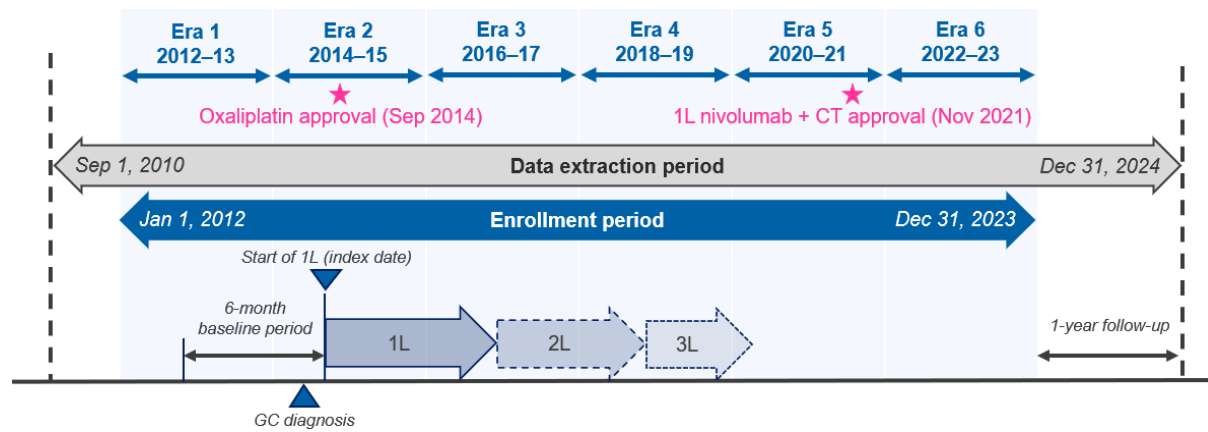
Characteristic	Overall N=7,895	Era 5 (2020–2021)			Era 6 (2022–2023)		
		Overall N=3,796	CT n=3,730	Nivo + CT n=66	Overall N=4,099	CT n=1,569	Nivo + CT n=2,530
Sex							
Male	5,709 (72.3)	2,770 (73.0)	2,720 (72.9)	50 (75.8)	2,939 (71.7)	1,149 (73.2)	1,790 (70.8)
Female	2,186 (27.7)	1,026 (27.0)	1,010 (27.1)	16 (24.2)	1,160 (28.3)	420 (26.8)	740 (29.2)
Number of beds in hospital							
<200	374 (4.7)	176 (4.6)	168 (4.5)	8 (12.1)	198 (4.8)	101 (6.4)	97 (3.8)
200–499	4,097 (51.9)	1,998 (52.6)	1,978 (53.0)	20 (30.3)	2,099 (51.2)	863 (55.0)	1,236 (48.9)
≥500	3,424 (43.4)	1,622 (42.7)	1,584 (42.5)	38 (57.6)	1,802 (44.0)	605 (38.6)	1,197 (47.3)
Designated cancer hospital ^b							
Yes	6,513 (82.5)	3,104 (81.8)	3,048 (81.7)	56 (84.8)	3,409 (83.2)	1,250 (79.7)	2,159 (85.3)
No	1,382 (17.5)	692 (18.2)	682 (18.3)	10 (15.2)	690 (16.8)	319 (20.3)	371 (14.7)
Age, median (range), years	72 (21, 93)	71 (21, 91)	71 (21, 91)	69 (38, 85)	72 (22, 93)	73 (29, 92)	72 (22, 93)
Age category, years							
<65	1,764 (22.3)	902 (23.8)	883 (23.7)	19 (28.8)	862 (21.0)	241 (15.4)	621 (24.5)
65–74	3,438 (43.5)	1,706 (44.9)	1,676 (44.9)	30 (45.5)	1,732 (42.3)	697 (44.4)	1,035 (40.9)
≥75	2,693 (34.1)	1,188 (31.3)	1,171 (31.4)	17 (25.8)	1,505 (36.7)	631 (40.2)	874 (34.5)
Metastasis site							
Peritoneal or ascites	1,929 (24.4)	967 (25.5)	942 (25.3)	25 (37.9)	962 (23.5)	286 (18.2)	676 (26.7)
Liver	1,422 (18.0)	733 (19.3)	717 (19.2)	16 (24.2)	689 (16.8)	241 (15.4)	448 (17.7)
Lymph node	1,262 (16.0)	632 (16.6)	619 (16.6)	13 (19.7)	630 (15.4)	229 (14.6)	401 (15.8)
Bone	302 (3.8)	148 (3.9)	144 (3.9)	4 (6.1)	154 (3.8)	46 (2.9)	108 (4.3)
Lung	266 (3.4)	129 (3.4)	126 (3.4)	3 (4.5)	137 (3.3)	58 (3.7)	79 (3.1)
Brain	26 (0.3)	15 (0.4)	14 (0.4)	1 (1.5)	11 (0.3)	6 (0.4)	5 (0.2)
Comorbidities							

Hypertension	2,200 (27.9)	1,032 (27.2)	1,020 (27.3)	12 (18.2)	1,168 (28.5)	471 (30.0)	697 (27.5)
Edema	169 (2.1)	72 (1.9)	72 (1.9)	0	97 (2.4)	35 (2.2)	62 (2.5)
Liver diseases	1,205 (15.3)	532 (14.0)	518 (13.9)	14 (21.2)	673 (16.4)	223 (14.2)	450 (17.8)
Renal disease	578 (7.3)	272 (7.2)	267 (7.2)	5 (7.6)	306 (7.5)	120 (7.6)	186 (7.4)
Diabetes	1,810 (22.9)	800 (21.1)	792 (21.2)	8 (12.1)	1,010 (24.6)	375 (23.9)	635 (25.1)
Thrombosis	654 (8.3)	279 (7.3)	274 (7.3)	5 (7.6)	375 (9.1)	135 (8.6)	240 (9.5)
Ischemic heart disease	490 (6.2)	204 (5.4)	202 (5.4)	2 (3.0)	286 (7.0)	126 (8.0)	160 (6.3)
Hemorrhoids	109 (1.4)	60 (1.6)	59 (1.6)	1 (1.5)	49 (1.2)	23 (1.5)	26 (1.0)
Neuropathy	245 (3.1)	106 (2.8)	103 (2.8)	3 (4.5)	139 (3.4)	51 (3.3)	88 (3.5)
CCI score							
0	55 (0.7)	26 (0.7)	25 (0.7)	1 (1.5)	29 (0.7)	12 (0.8)	17 (0.7)
1	5 (0.1)	1 (0.0)	1 (0.0)	0	4 (0.1)	0	4 (0.2)
2	3,032 (38.4)	1,440 (37.9)	1,425 (38.2)	15 (22.7)	1,592 (38.8)	677 (43.1)	915 (36.2)
3	217 (2.7)	100 (2.6)	97 (2.6)	3 (4.5)	117 (2.9)	51 (3.3)	66 (2.6)
≥4	4,586 (58.1)	2,229 (58.7)	2,182 (58.5)	47 (71.2)	2,357 (57.5)	829 (52.8)	1,528 (60.4)
ADL							
Dependent	569 (7.2)	266 (7.0)	264 (7.1)	2 (3.0)	303 (7.4)	129 (8.2)	174 (6.9)
Independent	5,529 (70.0)	2,676 (70.5)	2,630 (70.5)	46 (69.7)	2,853 (69.6)	1,062 (67.7)	1,791 (70.8)
Missing	1,774 (22.5)	853 (22.5)	835 (22.4)	18 (27.3)	921 (22.5)	374 (23.8)	547 (21.6)
Unknown	23 (0.3)	1 (0.0)	1 (0.0)	0	22 (0.5)	4 (0.3)	18 (0.7)
BMI category, kg/m ²							
<18.5	1,165 (19.2)	553 (19.0)	542 (18.9)	11 (22.9)	612 (19.5)	235 (19.9)	377 (19.2)
18.5–24.9	3,994 (65.9)	1,928 (66.1)	1,898 (66.1)	30 (62.5)	2,066 (65.8)	757 (64.2)	1,309 (66.8)
25–29.9	788 (13.0)	380 (13.0)	373 (13.0)	7 (14.6)	408 (13.0)	175 (14.8)	233 (11.9)
≥30	110 (1.8)	57 (2.0)	57 (2.0)	0	53 (1.7)	13 (1.1)	40 (2.0)
Missing	1,838	878	860	18	960	389	571

^aData are presented as n (%), unless otherwise stated; ^bDesignated cancer hospitals refers to a medical institution designated by Japan's Ministry of Health, Labour and Welfare to serve as a central facility for cancer treatment in Japan

ADL activities of daily living, *BMI* body mass index, *CCI* Charlson Comorbidity Index, *CT* chemotherapy, *Nivo* nivolumab, *SD* standard deviation

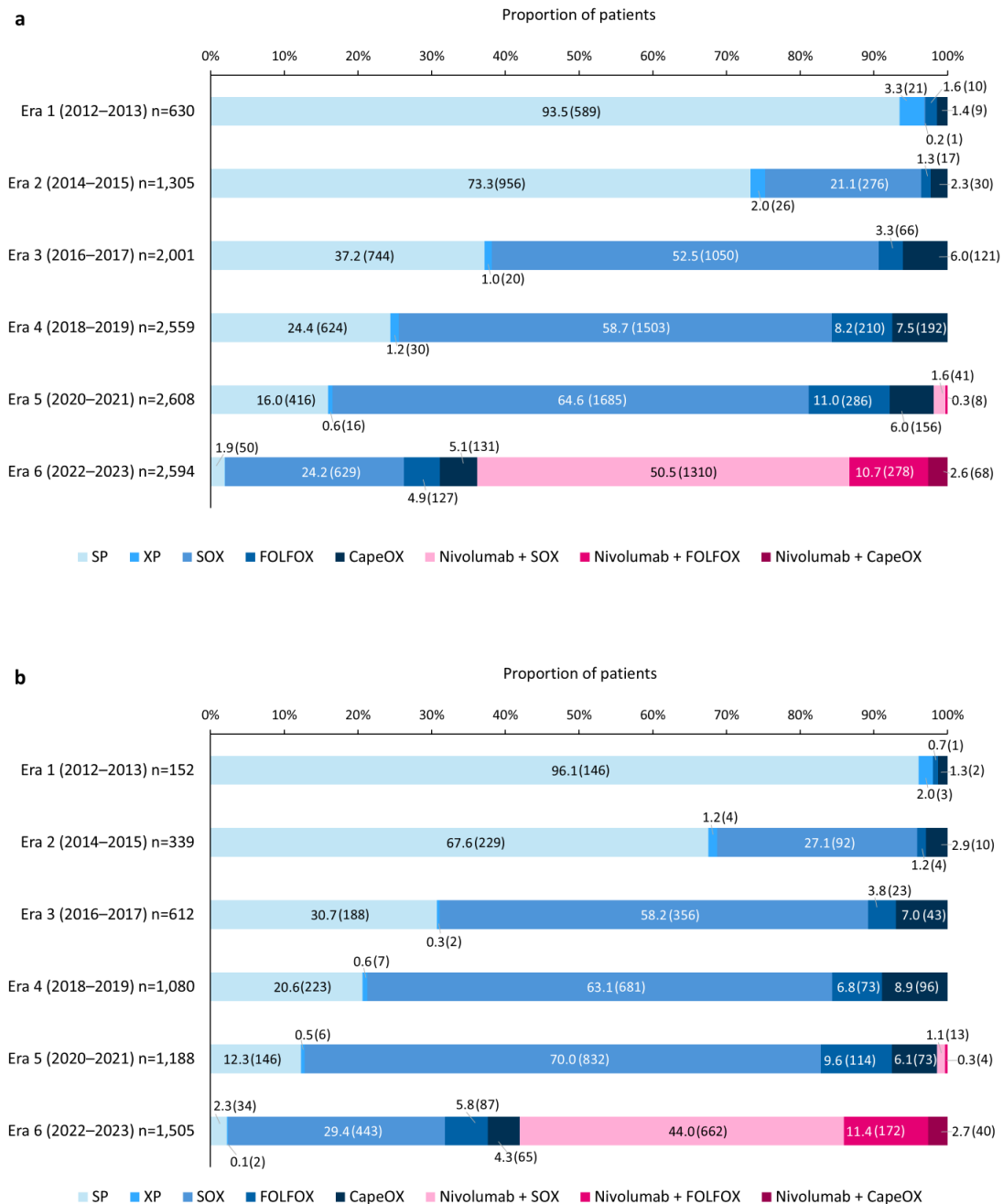
Supplementary Fig. S1 Study design for the primary and secondary analyses



Pink stars indicate approval dates in Japan

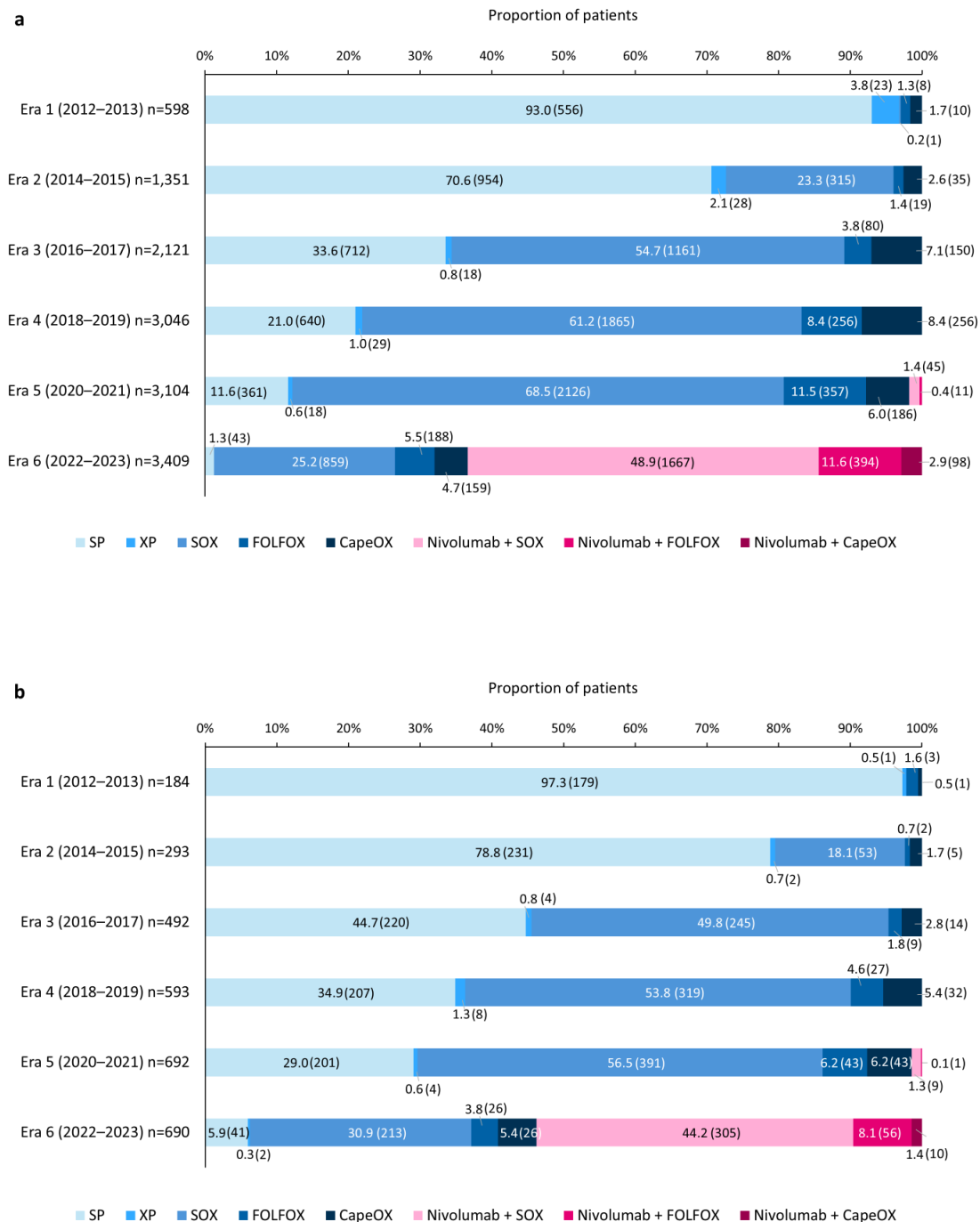
1L first-line, 2L second-line, 3L third-line, CT chemotherapy, GC gastric cancer, Nivo nivolumab

Supplementary Fig. S2 First-line treatment regimens in subgroups defined by patient age at index date: (a) <75 versus (b) ≥75 years. Numbers of patients are indicated in parentheses next to the percentage.



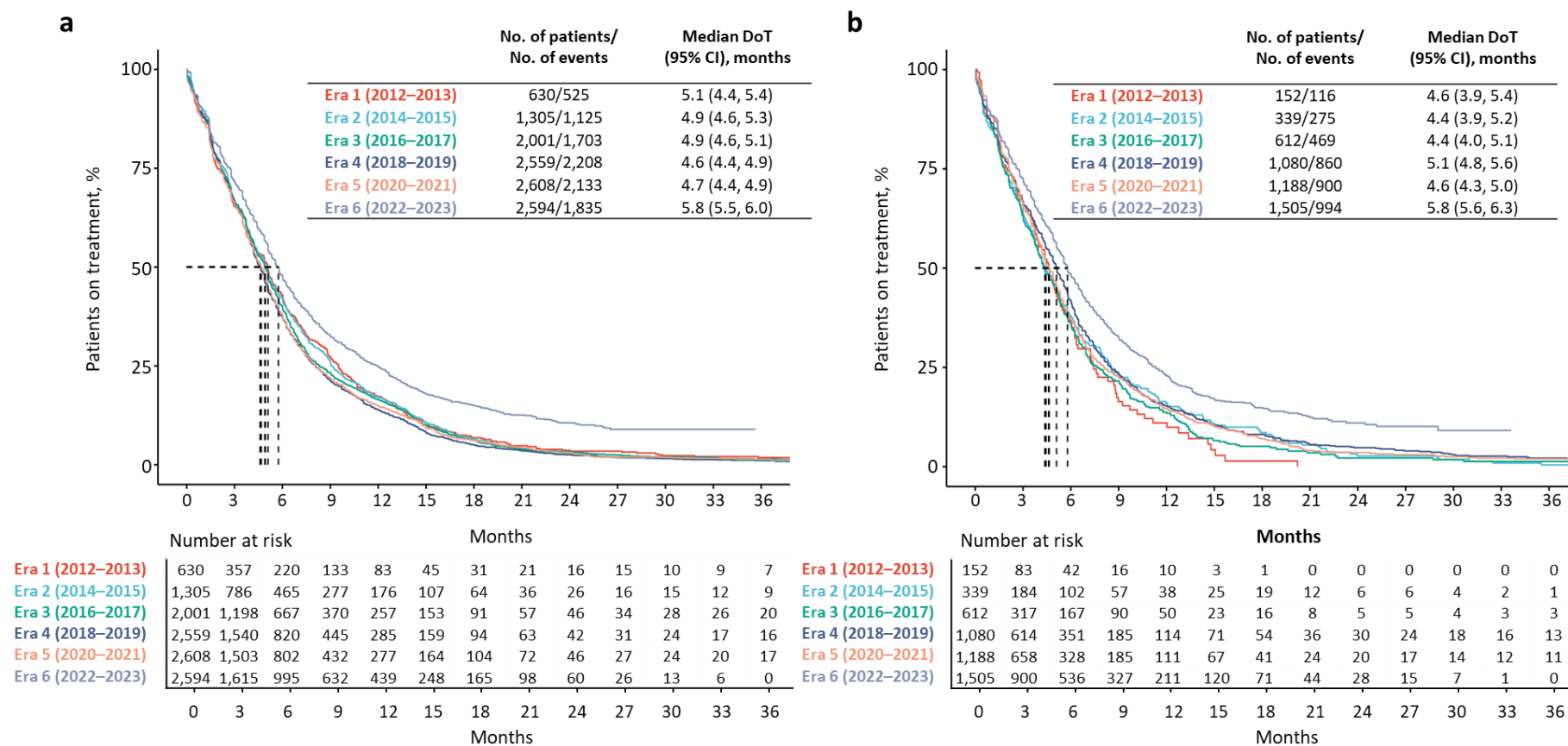
CapeOX capecitabine plus oxaliplatin, *FOLFOX* folinic acid + fluorouracil plus oxaliplatin, *S-1* tegafur plus gimeracil plus oteracil, *SOX* S-1 plus oxaliplatin, *SP* S-1 plus cisplatin, *XP* capecitabine plus cisplatin

Supplementary Fig. S3 First-line treatment patterns in subgroups defined by designated hospital: (a) designated cancer hospital vs (b) non-designated cancer hospital. Numbers of patients are indicated in parentheses next to the percentage.



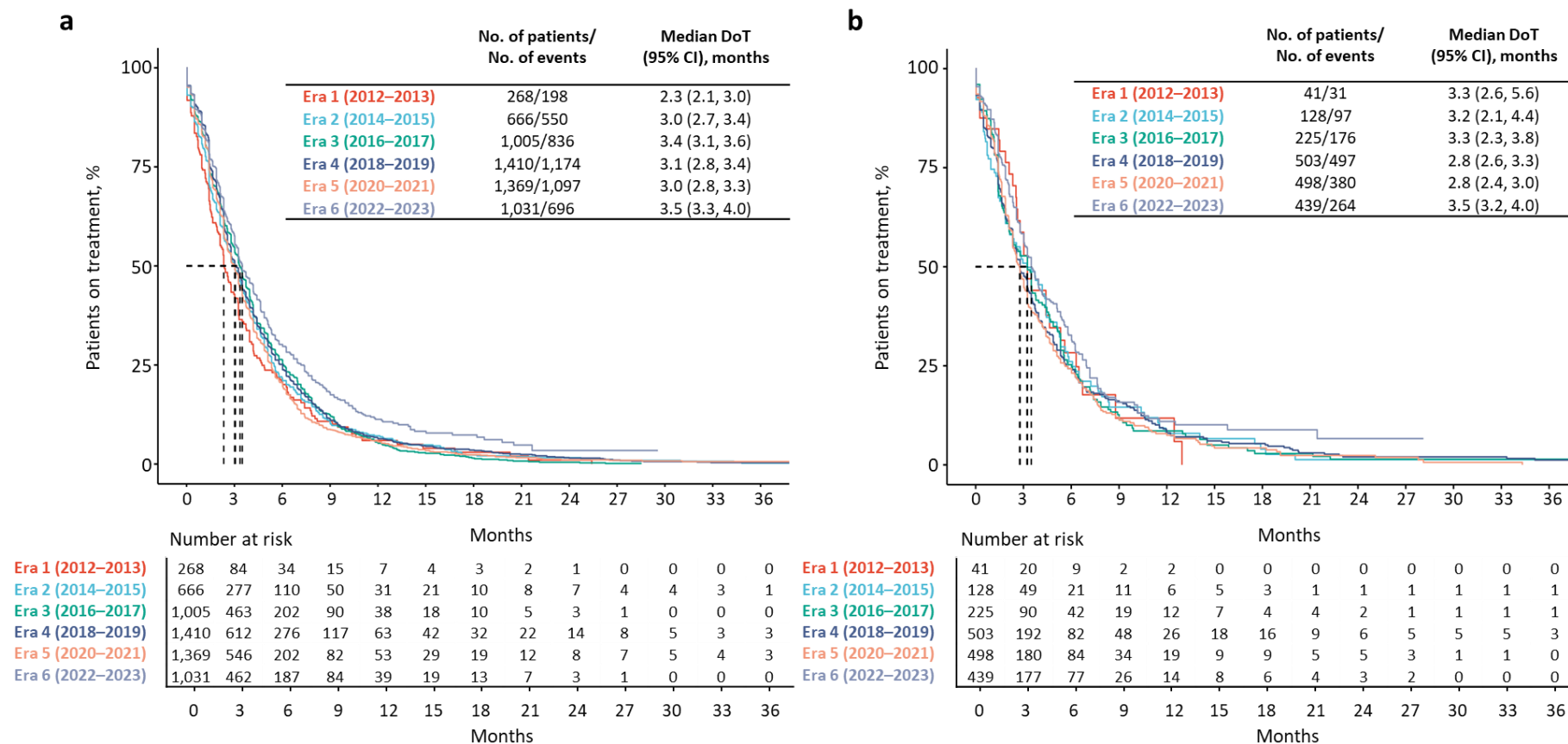
CapeOX capecitabine plus oxaliplatin, *FOLFOX* folinic acid-fluorouracil plus oxaliplatin, *S-1* tegafur plus gimeracil plus oteracil, *SOX* S-1 plus oxaliplatin, *SP* S-1 plus cisplatin, *XP* capecitabine plus cisplatin

Supplementary Fig. S4 First-line duration of therapy in subgroups defined by patient age at index date: (a) <75 years versus (b) ≥75 years



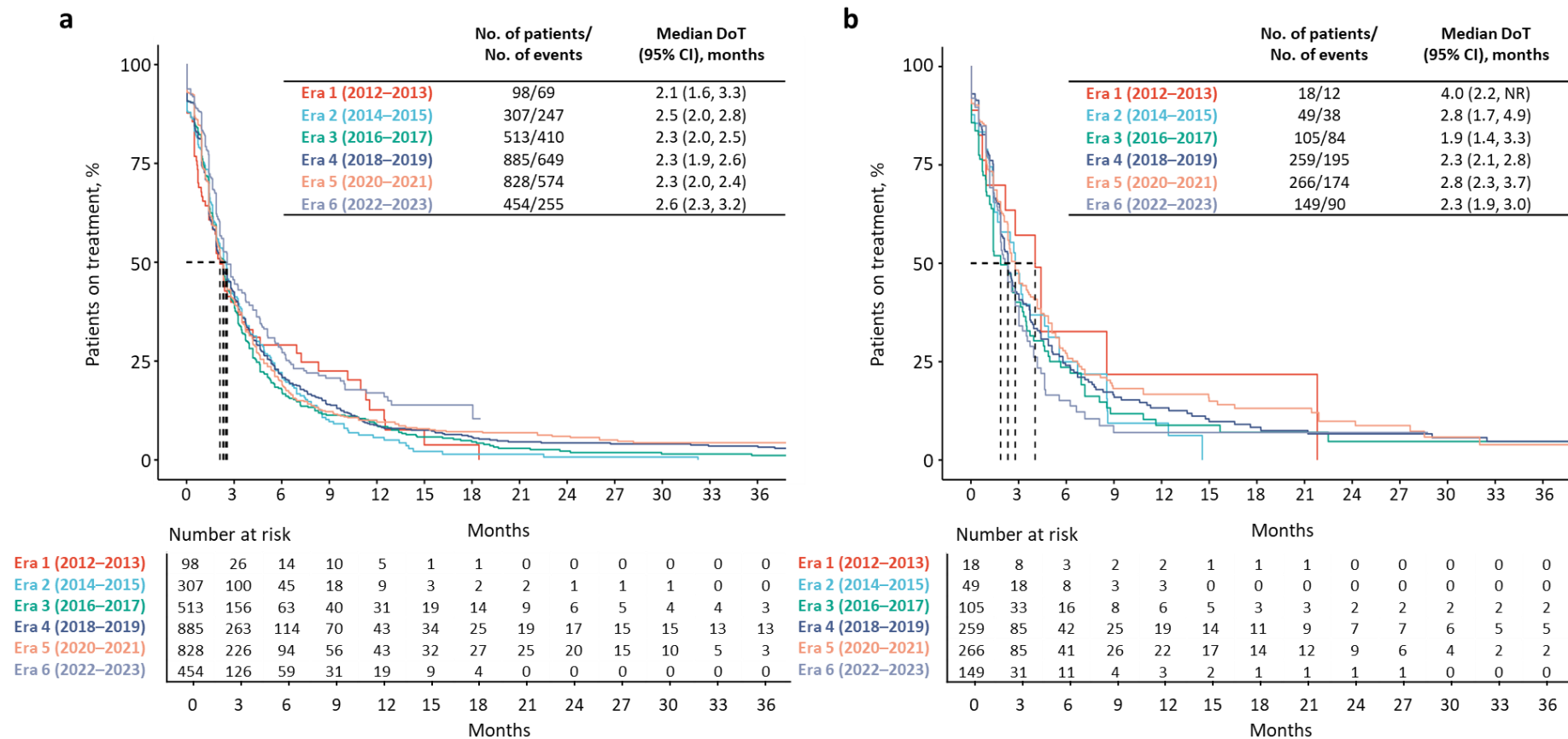
CI confidence interval, DoT duration of therapy

Supplementary Fig. S5 Second-line duration of therapy in subgroups defined by patient age at index date: (a) <75 years versus (b) ≥75 years



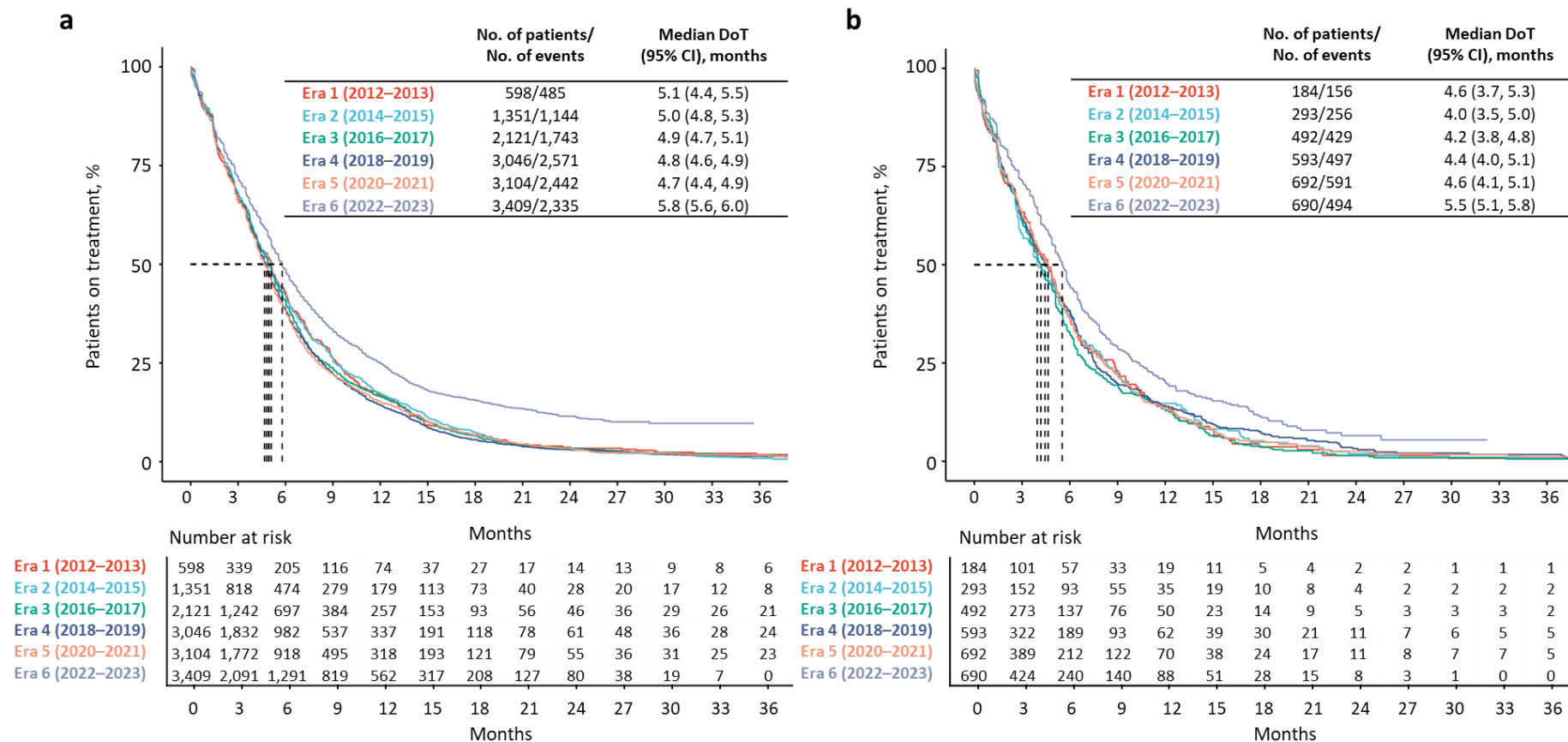
CI confidence interval, DoT duration of therapy

Supplementary Fig. S6 Third-line duration of therapy in subgroups defined by patient age at index date: (a) <75 years versus (b) ≥75 years



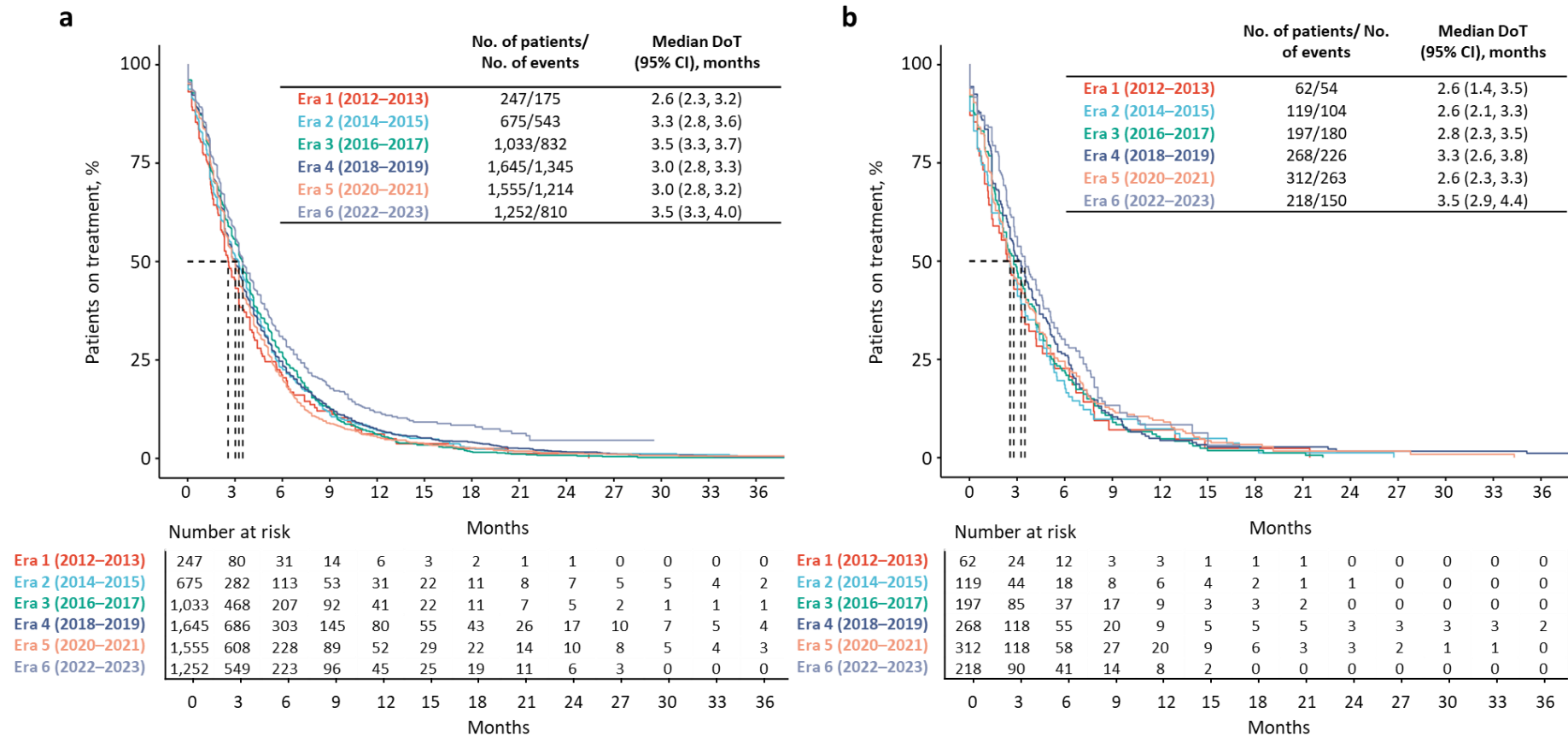
CI confidence interval, DoT duration of therapy, NR not reached

Supplementary Fig. S7 First-line duration of therapy in subgroups defined by treatment facility: (a) designated cancer hospital versus (b) non-designated cancer hospital



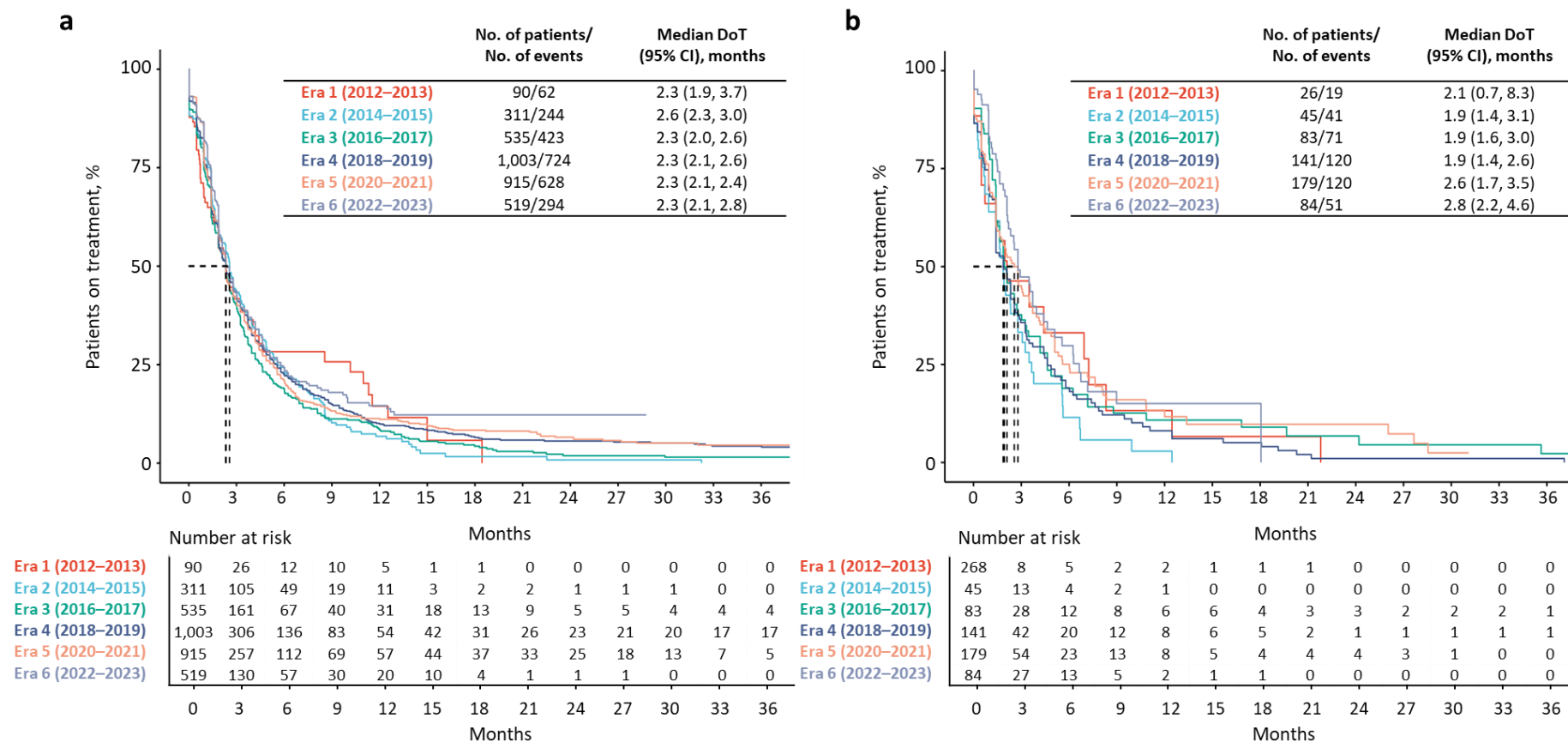
CI confidence interval, DoT duration of therapy

Supplementary Fig. S8 Second-line duration of therapy in subgroups defined by treatment facility: (a) designated cancer hospital vs (b) non-designated cancer hospital



CI confidence interval, DoT duration of therapy

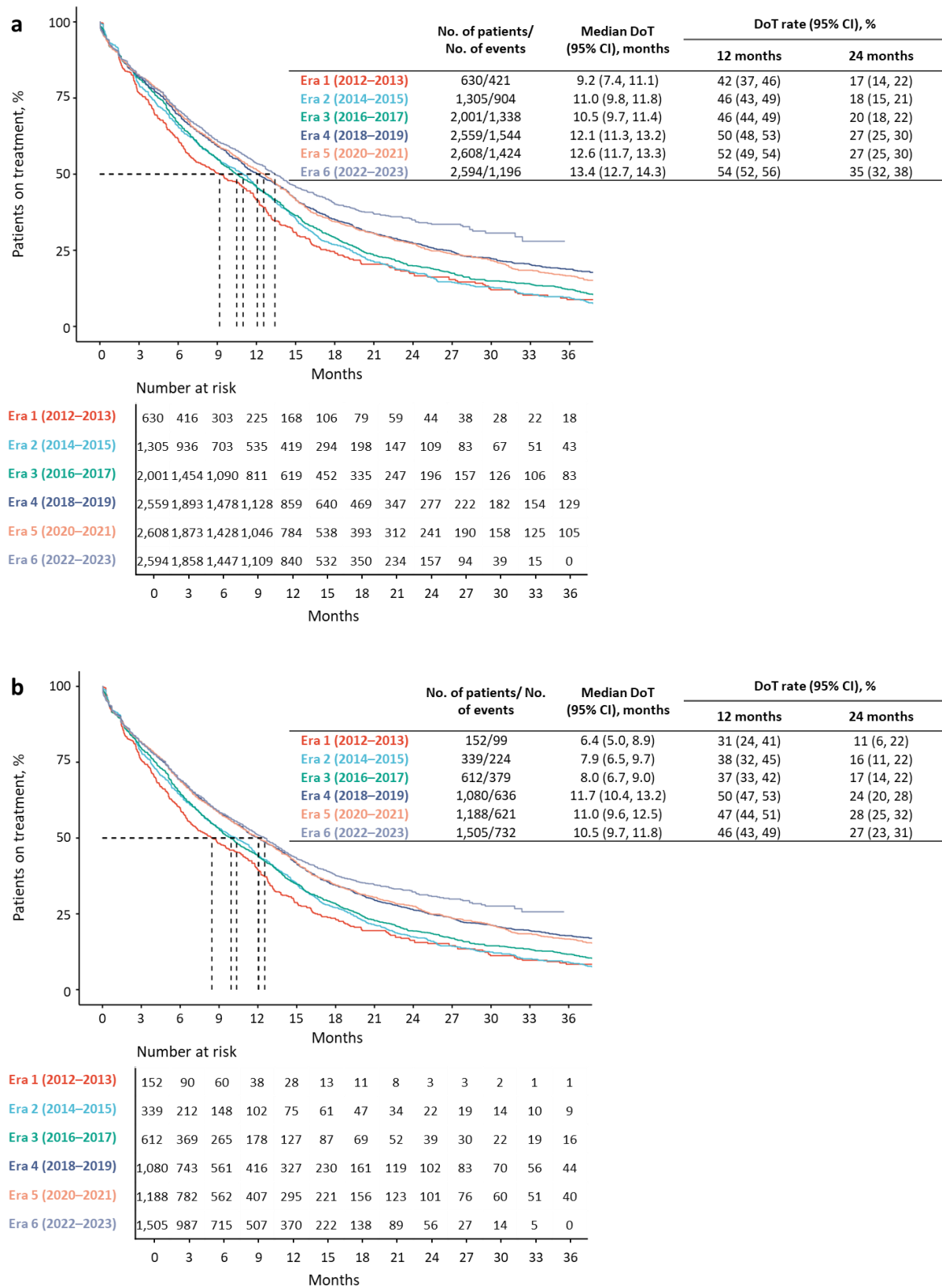
Supplementary Fig. S9 Third-line duration of therapy in subgroups defined by treatment facility: hospital (a) designated cancer hospital vs (b) non-designated cancer hospital



CI confidence interval, DoT duration of therapy

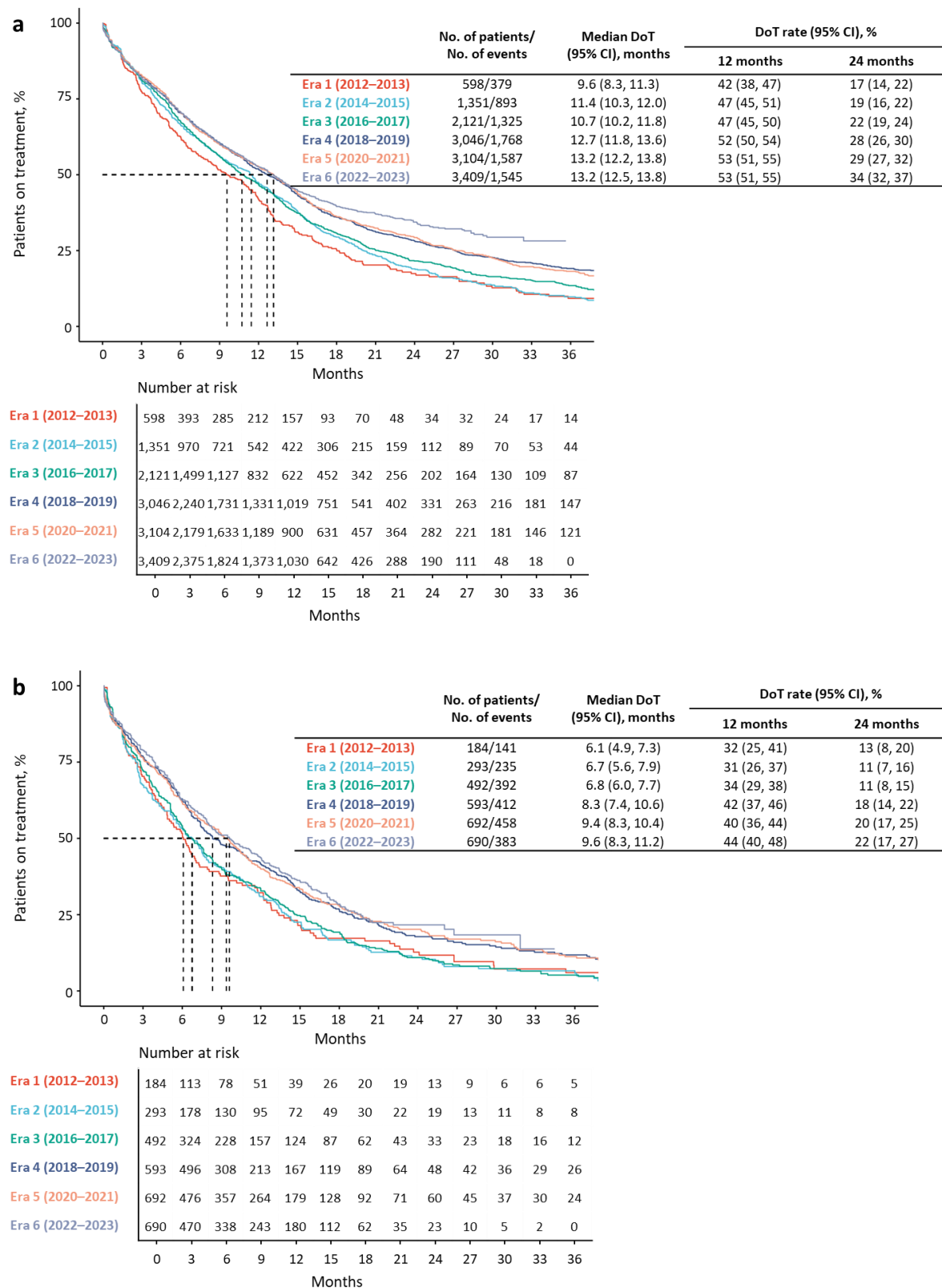
Supplementary Fig. S10 Overall duration of therapy in subgroups defined by patients age at index

date: (a) <75 years versus (b) ≥75 years



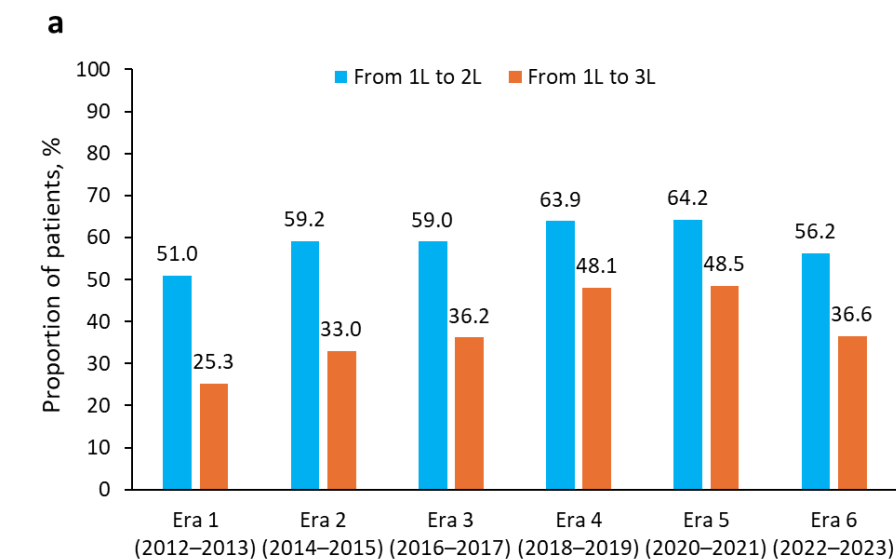
1L first-line, CI confidence interval, DoT duration of therapy

Supplementary Fig. S11 Overall duration of therapy in subgroups defined by treatment facility: (a) designated cancer hospital vs (b) non-designated cancer hospital

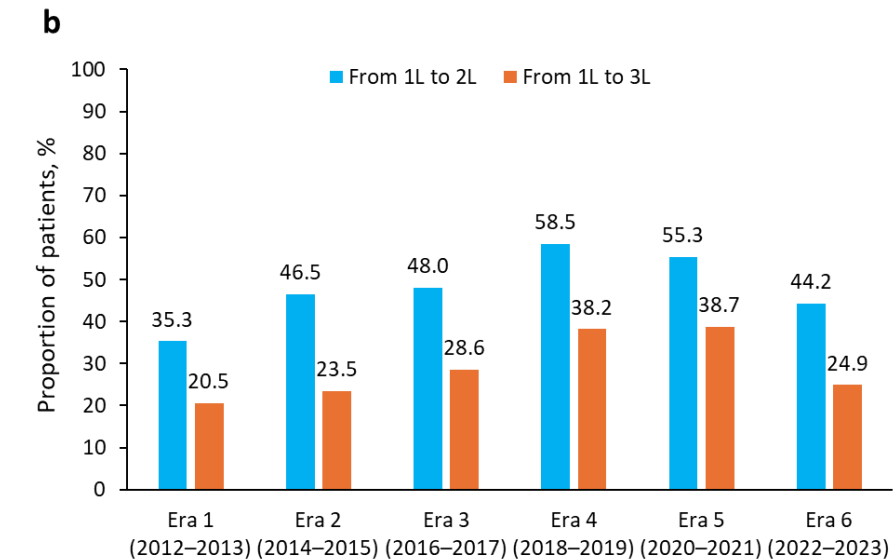


CI confidence interval, DoT duration of therapy

Supplementary Fig. S12 Transition rates from first-line to later lines of treatment in subgroups defined by patient age at index date: (a) <75 years vs (b) ≥75 years



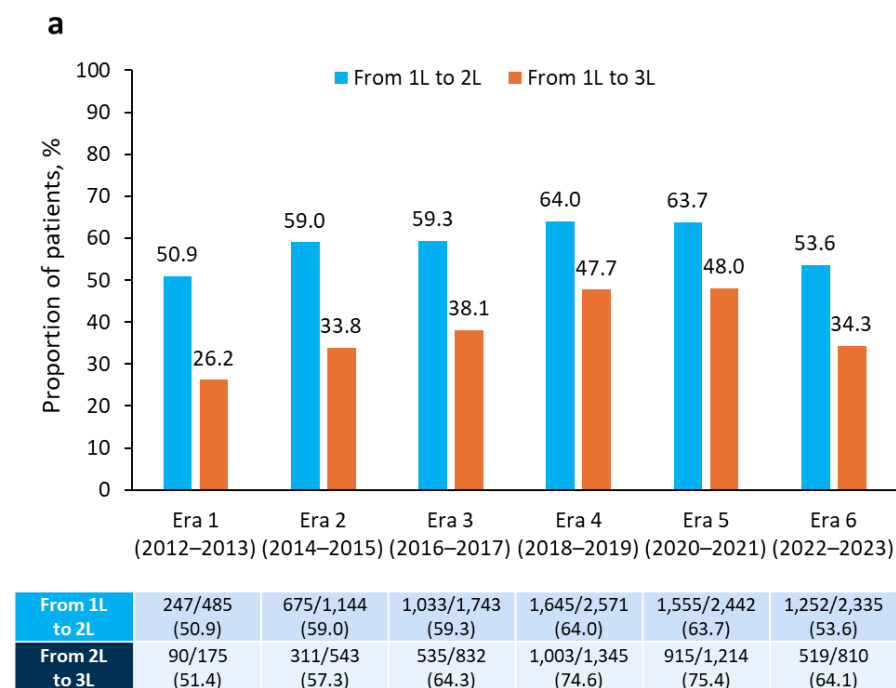
From 1L to 2L	268/525 (51.0)	666/1,125 (59.2)	1,005/1,703 (59.0)	1,410/2,208 (63.9)	1,369/2,133 (64.2)	1,031/1,835 (56.2)
From 2L to 3L	98/198 (49.5)	307/550 (55.8)	513/836 (61.4)	885/1,174 (75.4)	828/1097 (75.5)	454/696 (65.2)



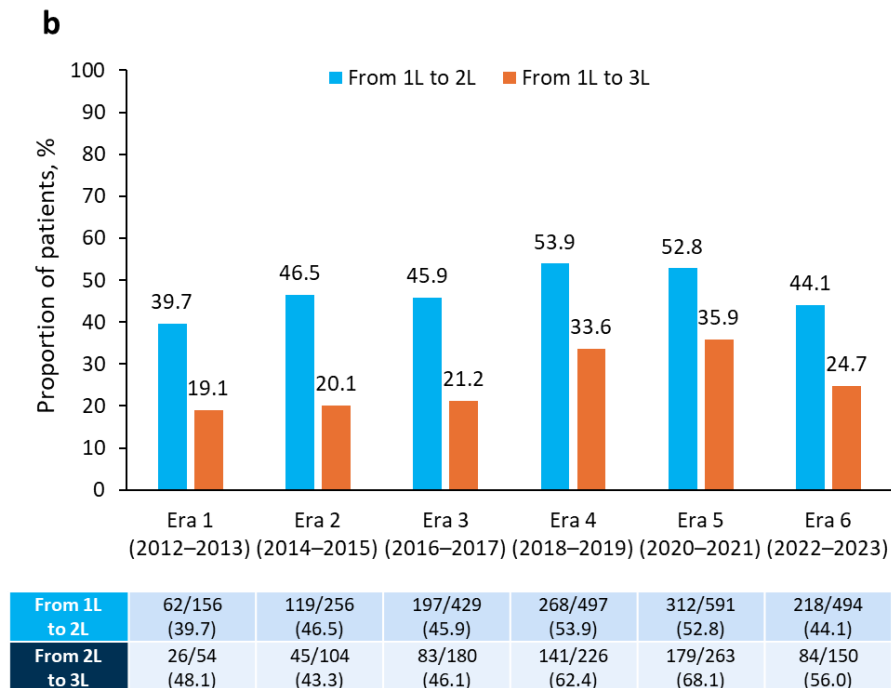
From 1L to 2L	41/116 (35.3)	128/275 (46.5)	225/469 (48.0)	503/860 (58.5)	498/900 (55.3)	439/994 (44.2)
From 2L to 3L	18/31 (58.1)	49/97 (50.5)	105/176 (59.7)	259/397 (65.2)	266/380 (70.0)	149/264 (56.4)

1L first-line, 2L second-line, 3L third-line

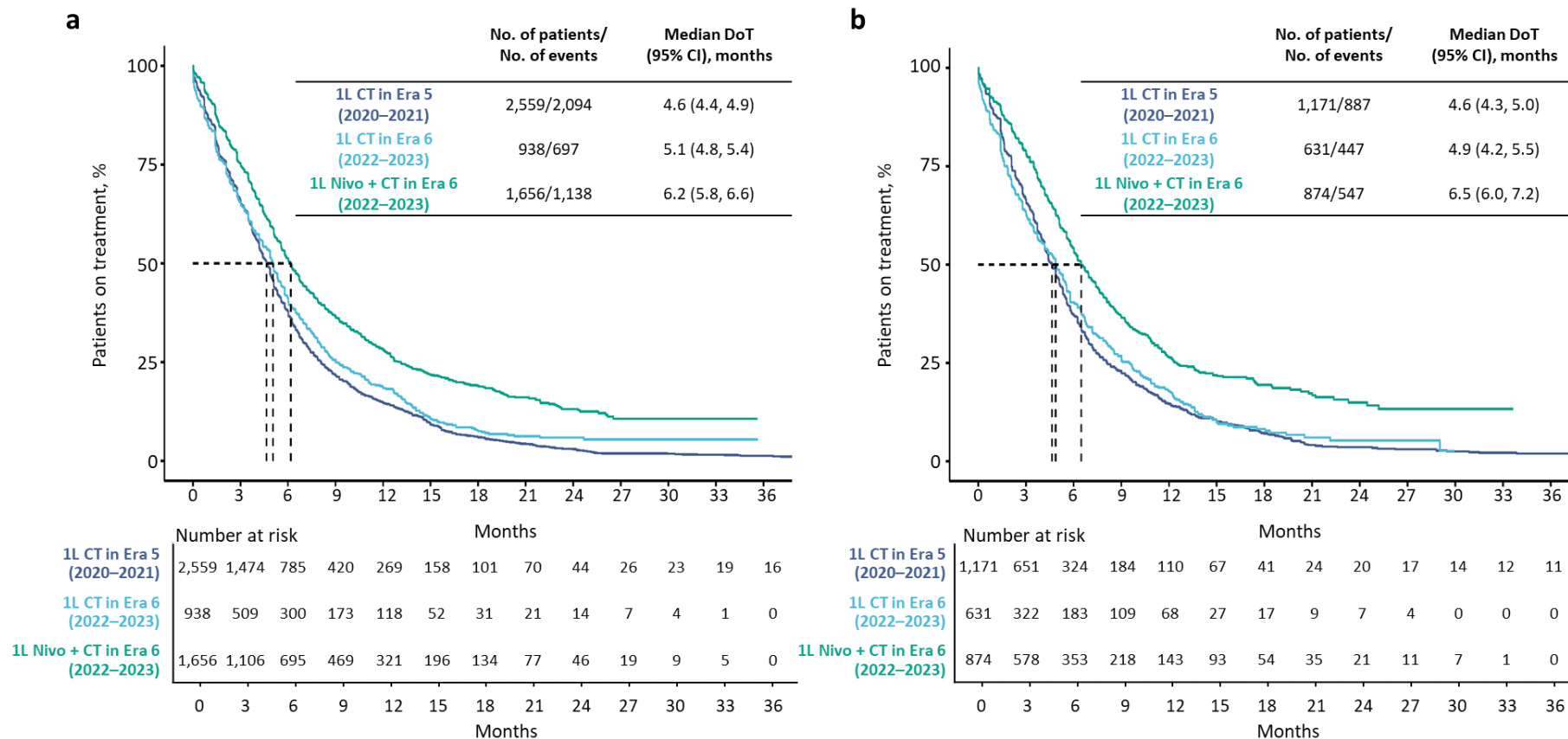
Supplementary Fig. S13 Transition rates from first-line to later lines of treatment in subgroups defined by treatment facility: (a) designated cancer hospital vs (b) non-designated cancer hospital



1L first-line, 2L second-line, 3L third-line

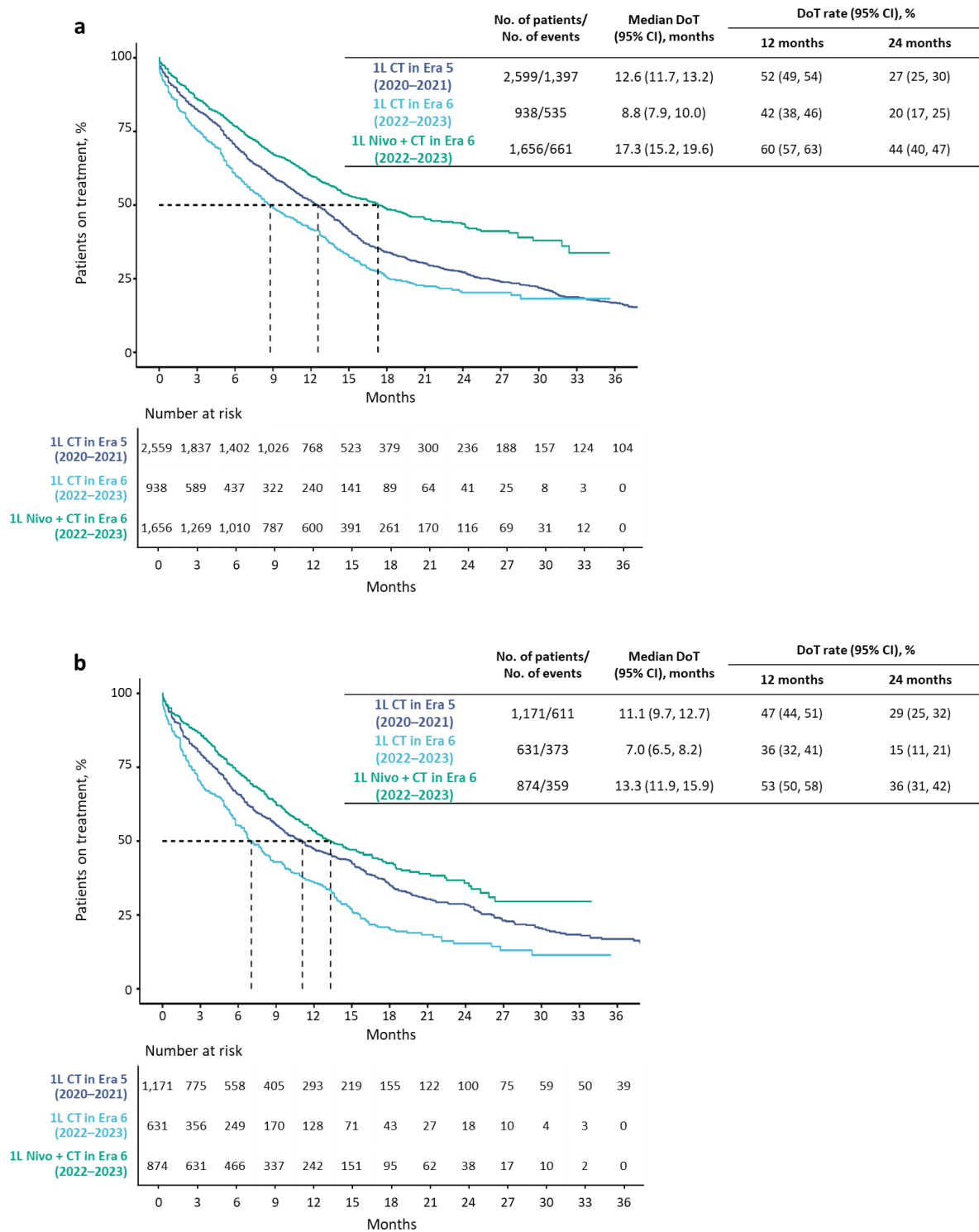


Supplementary Fig. S14 First-line duration of therapy for nivolumab plus chemotherapy in Era 6 (2022–2023) vs chemotherapy in Era 5 (2020–2021) and Era 6 (2022–2023) in subgroups defined by patient age at index date: (a) <75 years vs (b) ≥75 years



CI confidence interval, CT chemotherapy, DoT duration of therapy, Nivo nivolumab

Supplementary Fig. S15 Overall duration of therapy for nivolumab plus chemotherapy in Era 6 (2022–2023) vs chemotherapy in Era 5 (2020–2021) and Era 6 (2022–2023) in subgroups defined by patient age at index date: (a) <75 years vs (b) ≥75 years



CI confidence interval, CT chemotherapy, DoT duration of therapy, Nivo nivolumab

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1. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2021 (6th edition). *Gastric Cancer*. 2023;26(1):1–25.
2. Wade DT, Collin C. The Barthel ADL Index: a standard measure of physical disability? *Int Disabil Stud*. 1988;10(2):64–7.