Supplementary Online Content

Yap DWT, Leone AG, Wong NZH, et al. Efficacy of immune checkpoint inhibitors in patients with advanced esophageal squamous cell carcinoma: a meta-analysis including low PD-L1 subgroups. *JAMA Oncol*. Published online December 8, 2022. doi:10.1001/jamaoncol.2022.5816

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Search Information

Date of search	1 October 2021
Databases	PubMed, Web of Science, Scopus, Embase, American Society of Clinical Oncology Meeting Library
Search string	(gastric OR stomach OR esophageal OR gastroesophageal OR gastro-oesophageal OR gastro-esophageal) AND (checkpoint inhibitors OR ICI OR pembrolizumab OR ipilimumab OR nivolumab OR avelumab OR camrelizumab OR durvalumab OR sintilimab OR programmed death ligand OR "PD-L1" OR "PD-1" OR immunotherapy) AND (random* AND trial)
Search string exploded	("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields] OR ("stomach"[MeSH Terms] OR "stomach"[All Fields] OR "stomachs"[All Fields] OR "stomach s"[All Fields] OR "stomachal"[All Fields] OR "stomaches"[All Fields]) OR ("esophageal"[All Fields] OR "esophagic"[All Fields] OR "esophagitis"[MeSH Terms] OR "esophagitis"[All Fields] OR "esophagitides"[All Fields] OR "oesophagal"[All Fields] OR "oesophageal"[All Fields] OR "oesophagic"[All Fields] OR "oesophagitis"[All Fields]) OR ("gastro esophageal"[All Fields] OR "gastro oesophageal"[All Fields] OR "gastro oesophagitis"[All Fields] OR "gastroesophagal"[All Fields] OR "gastroesophageal"[All Fields] OR "gastroesophagic"[All Fields] OR "gastroesophagitis"[All Fields] OR "gastrooesophageal"[All Fields]) OR ("gastro esophageal"[All Fields] OR "gastro oesophageal"[All Fields] OR "gastro oesophagitis"[All Fields] OR "gastroesophagal"[All Fields] OR "gastroesophageal"[All Fields] OR "gastroesophagic"[All Fields] OR "gastroesophagitis"[All Fields] OR "gastrooesophageal"[All Fields]) OR ("gastro esophageal"[All Fields] OR "gastro oesophageal"[All Fields] OR "gastro oesophagitis"[All Fields] OR "gastroesophagal"[All Fields] OR "gastroesophageal"[All Fields] OR "gastroesophagic"[All Fields] OR "gastroesophagitis"[All Fields] OR "gastrooesophageal"[All Fields])) AND ((("cell cycle checkpoints"[MeSH Terms] OR ("cell"[All Fields] AND "cycle"[All Fields] AND "checkpoints"[All Fields]) OR "cell cycle checkpoints"[All Fields] OR "checkpoint"[All Fields] OR "checkpoints"[All Fields]) AND ("antagonists and inhibitors"[MeSH Subheading] OR ("antagonists"[All Fields] AND "inhibitors"[All Fields]) OR "antagonists and inhibitors"[All Fields] OR "inhibitors"[All Fields] OR "inhibitor"[All Fields] OR "inhibitor s"[All Fields])) OR "ICI"[All Fields] OR ("pembrolizumab"[Supplementary Concept] OR "pembrolizumab"[All Fields]) OR ("ipilimumab"[MeSH Terms] OR "ipilimumab"[All Fields]) OR ("nivolumab"[MeSH Terms] OR "nivolumab"[All Fields] OR "nivolumab s"[All Fields]) OR ("avelumab"[Supplementary Concept] OR "avelumab"[All Fields]) OR ("camrelizumab"[Supplementary Concept] OR "camrelizumab"[All Fields]) OR ("durvalumab"[Supplementary Concept] OR "durvalumab"[All Fields]) OR ("sintilimab"[Supplementary Concept] OR "sintilimab"[All Fields]) OR (("program"[All Fields] OR "program s"[All Fields] OR "programe"[All Fields] OR "programed"[All Fields] OR "programes"[All Fields] OR "programing"[All Fields] OR "programmability"[All Fields] OR "programmable"[All Fields] OR "programmably"[All Fields] OR "programme"[All Fields] OR "programme s"[All Fields] OR "programmed"[All Fields] OR "programmer"[All Fields] OR "programmer s"[All Fields] OR "programmers"[All Fields] OR "programmes"[All Fields] OR "programming"[All Fields] OR "programmings"[All Fields] OR "programs"[All Fields]) AND ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields]) AND ("ligand s"[All Fields] OR "liganded"[All Fields] OR "liganding"[All Fields] OR "ligands"[MeSH Terms] OR "ligands"[All Fields] OR "ligand"[All Fields])) OR "PD-L1"[All Fields] OR "PD-1"[All Fields] OR ("immunotherapy"[MeSH Terms] OR "immunotherapy"[All Fields] OR "immunotherapies"[All Fields] OR "immunotherapy s"[All Fields])) AND ("random*"[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "trial"[All Fields] OR "trial s"[All Fields] OR "trialed"[All Fields] OR "trialing"[All Fields] OR "trials"[All Fields]))

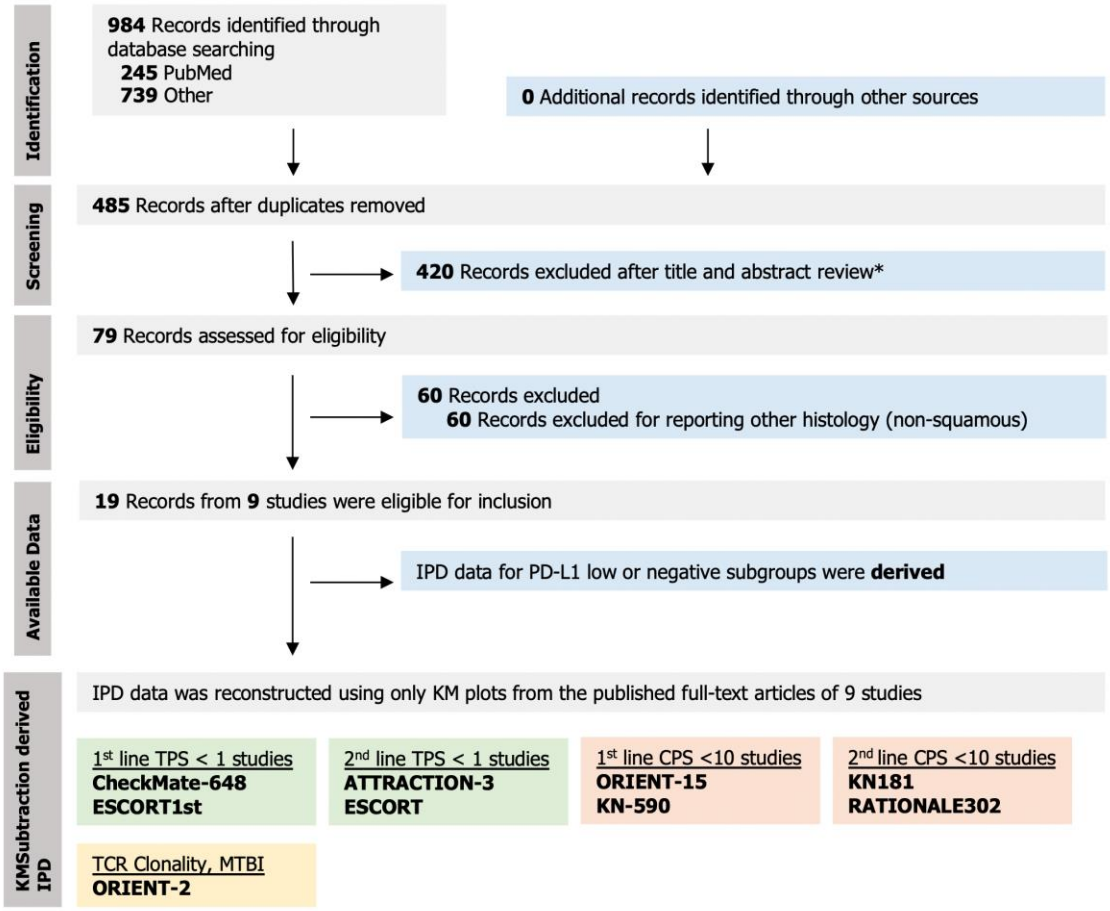
eTable 2. Search Information and Where KMSubtraction Was Implemented

Trial,	PD-L1 assay and reporting method	Comparison	Outcome	Histology	"Overall" curve	"Subgroup" High PD-L1 expressing curve	Did the original publication report the low PD-L1 KM curve?	Did the original publication report the low PD-L1 Hazard ratio?	PD-L1 low curves derived by KMSubtraction: i.e. "Subtracting" "Subgroup" curve from "overall" curve
ATTRACTION-3 Kato, 2019 NCT02569242	TPS ≥1 :Positive for PD-L1 when cancerous cells with stained cell membranes account for ≥1% of at least 100 evaluable cancerous cells IHC 28-8 pharmDx assay (Dako, Santa Clara, CA, USA)	Nivo/Chemo	OS	ESCC	Overall	PD-L1 TPS ≥1	Yes	Yes	NIL as originally reported in manuscript
CheckMate-648 Yuichiro, 2022 NCT03143153	TPS ≥ 1%: Percentage of tumor cells with partial or complete membrane staining in at least 100 viable TCs IHC 28-8 pharmDx assay (Dako, Santa Clara, CA, USA) *CPS also was retrospectively generated in the original trial. However, main KM curves were stratified based on TPS only	Nivo+Chemo/Chemo	OS	ESCC	Overall	PD-L1 TPS ≥1	No	Yes	PD-L1 TPS <1
		Nivo+Ipi/Chemo	OS	ESCC	Overall	PD-L1 TPS ≥1	No	Yes	PD-L1 TPS <1
		Nivo+Chemo/Chemo	PFS	ESCC	Overall	PD-L1 TPS ≥1	No	Yes	PD-L1 TPS <1
		Nivo+Ipi/Chemo	PFS	ESCC	Overall	PD-L1 TPS ≥1	No	Yes	PD-L1 TPS <1
		Nivo+Chemo/Chemo	DOR	ESCC	Overall	PD-L1 TPS ≥1	No	NA	PD-L1 TPS <1
		Nivo+Ipi/Chemo	DOR	ESCC	Overall	PD-L1 TPS ≥1	No	NA	PD-L1 TPS <1
ESCORT Huang, 2020 NCT03099382	TPS ≥1%: Percentage of viable tumor cells showing partial or complete membrane staining IHC 6E8 Abcam (Shuwen Biotech, Deqing, Zhejiang, China)	Camre/Chemo	OS	ESCC	Overall	PD-L1 TPS ≥1	No	Yes	PD-L1 TPS <1
ESCORT 1st Luo, 2021 NCT03691090	TPS ≥1%: Percentage of viable tumor cells showing partial or complete membrane staining, relative to all viable tumor cells present in the sample (positive and negative) IHC 6E8 Abcam (Shuwen Biotech, Deqing, Zhejiang, China)	Camre+Chemo/ Chemo	OS	ESCC	Overall	PD-L1 TPS ≥1	Yes	Yes	NIL as originally reported in manuscript
		Camre+Chemo/ Chemo	PFS	ESCC	Overall	PD-L1 TPS ≥1	Yes	Yes	NIL as originally reported in manuscript
		Camre+Chemo/ Chemo	DOR	ESCC	Overall	PD-L1 TPS ≥1	Yes	NA	NIL as originally reported in manuscript

KN181 Kojima, 2020 NCT02559687	CPS: defined as the number of PD-L1–positive cells (tumor cells, macrophages, and lymphocytes) divided by the total number of tumor cells, multiplied by 100 IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA)	Pembro/Chemo	OS	ESCC	Overall	PD-L1 CPS ≥10	No	Yes	PD-L1 CPS <10
KN590 Sun, 2021 NCT03189719	CPS: defined as the number of PD-L1–positive cells (tumor cells, macrophages, and lymphocytes) divided by the total number of tumor viable cells IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA)	Pembro+Chemo/Chemo	OS	ESCC	Overall	PD-L1 CPS ≥10	No	No	PD-L1 CPS <10
ORIENT-2 Xu, 2022 NCT03116152	IHC 22C3 pharmDx assay (Dako, Santa Clara, CA, USA) *Results for CPS and TPS subgroups were reported as hazard ratios only. Curves were only stratified based on NLR/ TCR clonality.	Sinti/Chemo	OS	ESCC	Overall	KM curves not reported (only HRs presented)	No	No	Not possible as only overall curve published, PD-L1 high subgroup curve not reported
ORIENT-15 Lu, 2022 NCT03748134	CPS: defined as the number of PD-L1 staining cells (tumor cells, macrophages, and lymphocytes) divided by the total number of tumor cells IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA)	Sinti+Chemo/Chemo	OS	ESCC	Overall	PD-L1 CPS ≥10	No	Yes	PD-L1 CPS <10
		Sinti+Chemo/Chemo	PFS	ESCC	Overall	PD-L1 CPS ≥10	No	Yes	PD-L1 CPS <10
		Sinti+Chemo/Chemo	DOR	ESCC	Overall	PD-L1 CPS ≥10	No	NA	PD-L1 CPS <10
RATIONALE 302 Lin, 2022 NCT03430843	TAP: Total percentage of the tumor area covered by tumor cells with any membrane staining above background and tumor-associated immune cells with any staining above background. IHC SP263 assay (Ventana)	Tisle/Chemo	OS	ESCC	Overall	PD-L1 TAP ≥10	Yes	Yes	NIL as originally reported in manuscript

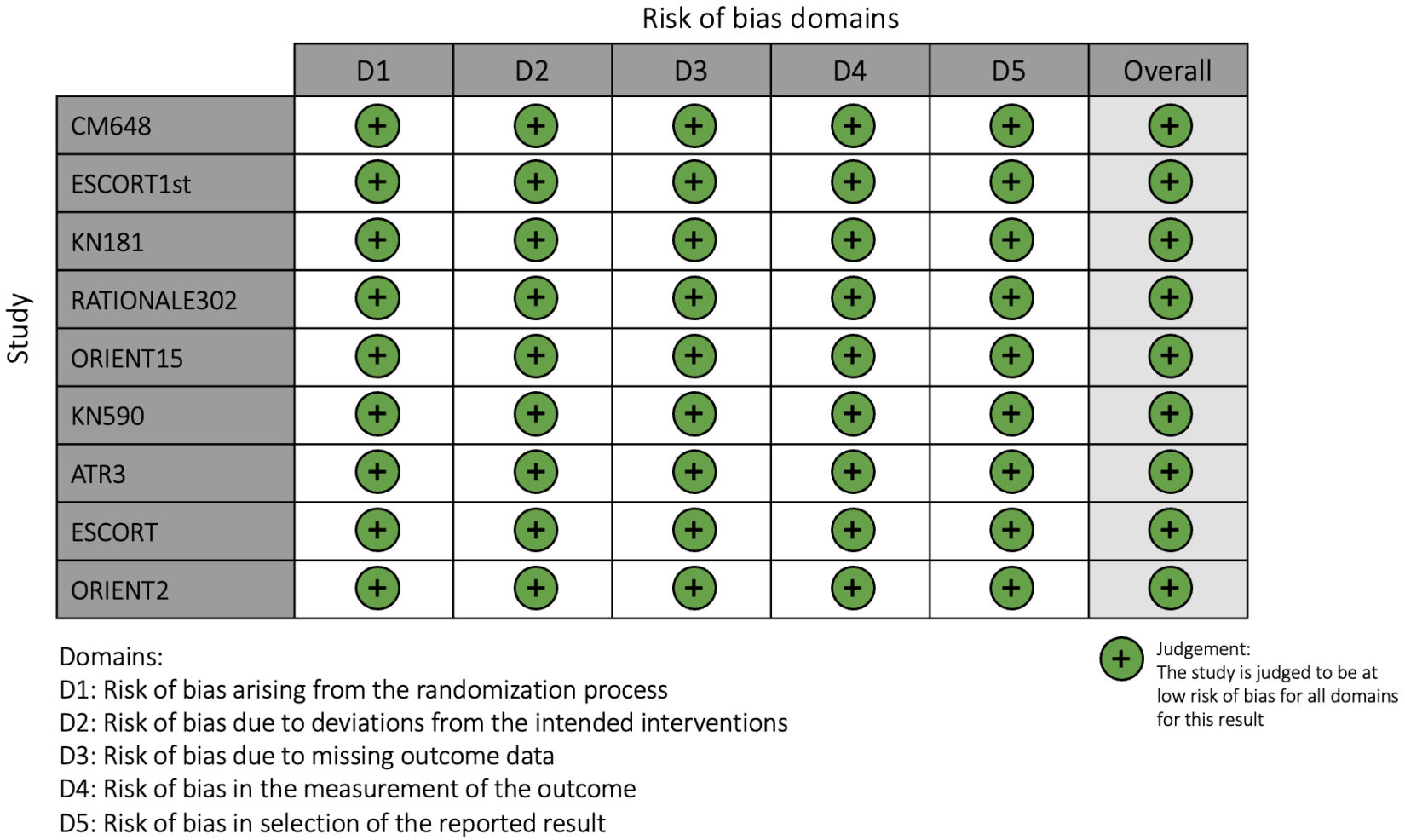
Abbreviations: Nivo, nivolumab; Ipi, ipilimumab; Camre, camrelizumab; Pembro, pembrolizumab; Sinti, sintilimab; Tisle, Tislelizumab; Chemo, chemotherapy; PD-L1, programmed death ligand 1; ESCC, esophageal squamous cell carcinoma; CPS, combined positive score; TPS, tumor proportion score; TAP, tumor area positivity; CM648, CheckMate 648; KN590, KEYNOTE-590; KN181, KEYNOTE-181.

eFigure 1. PRISMA Diagram



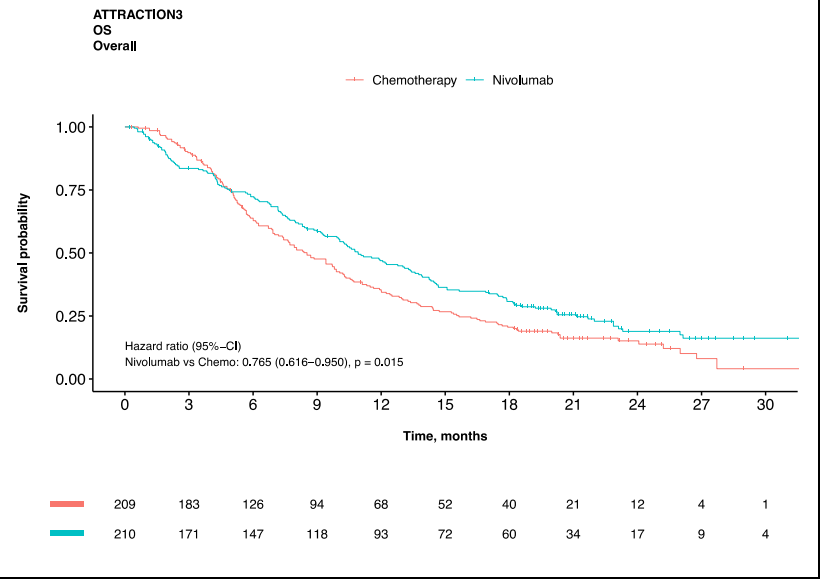
PRISMA, preferred reporting items for systematic reviews and meta-analyses; PD-L1, programmed death ligand 1; CPS, combined positive score; TPS, Tumor Proportion Score; IPD, individual patient data; KM, Kaplan-Meier; ESCC, esophageal squamous cell carcinoma; TCR, T-Cell Receptor; MTBI, Molecular Tumor Burden Index

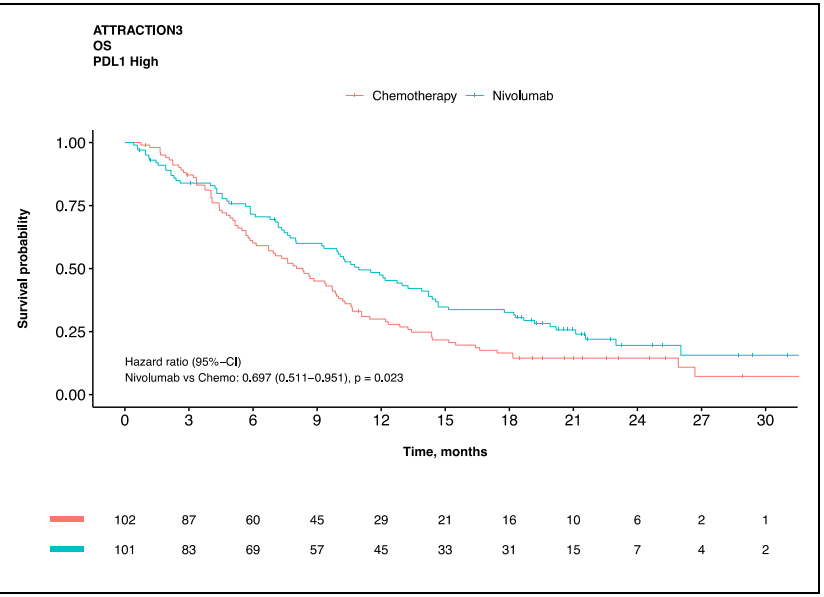
eFigure 2. Risk-of-Bias Assessment

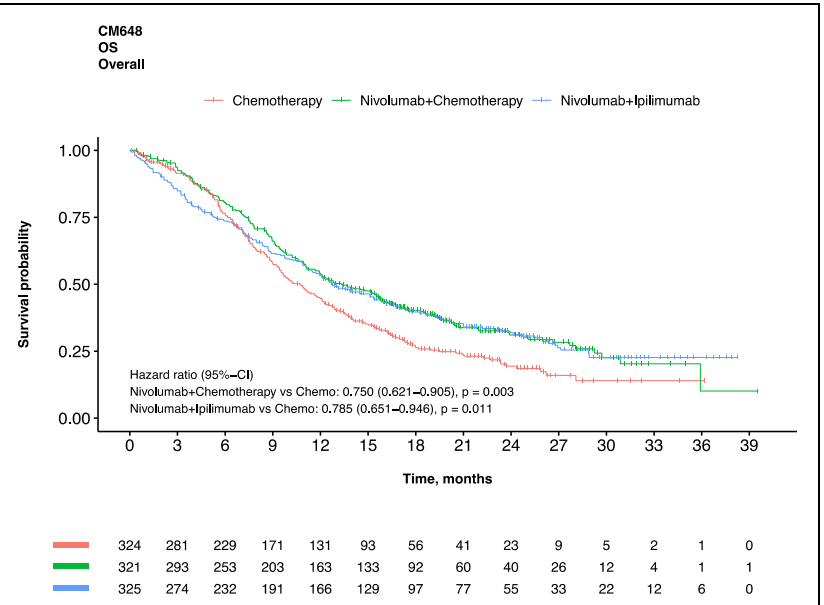


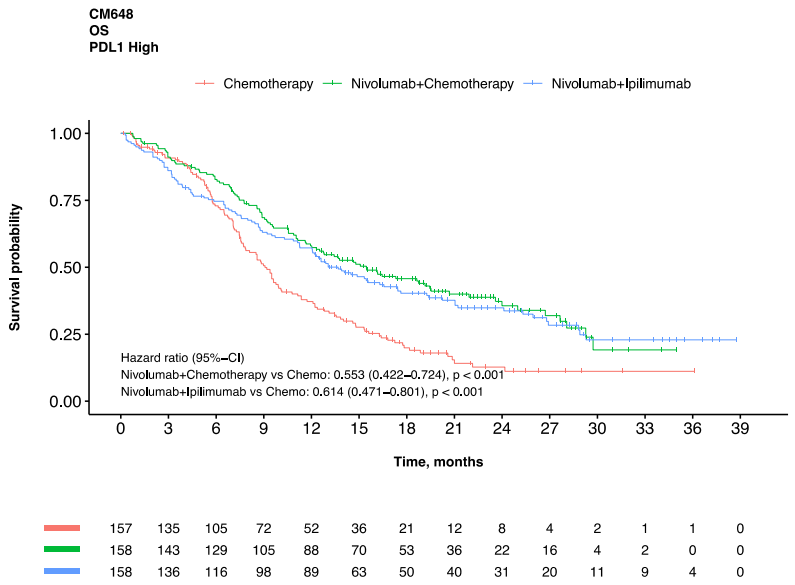
D, domain; CM648, CheckMate-648; KN181, KEYNOTE-181; KN590, KEYNOTE-590; ATR3, ATTRACTION-3

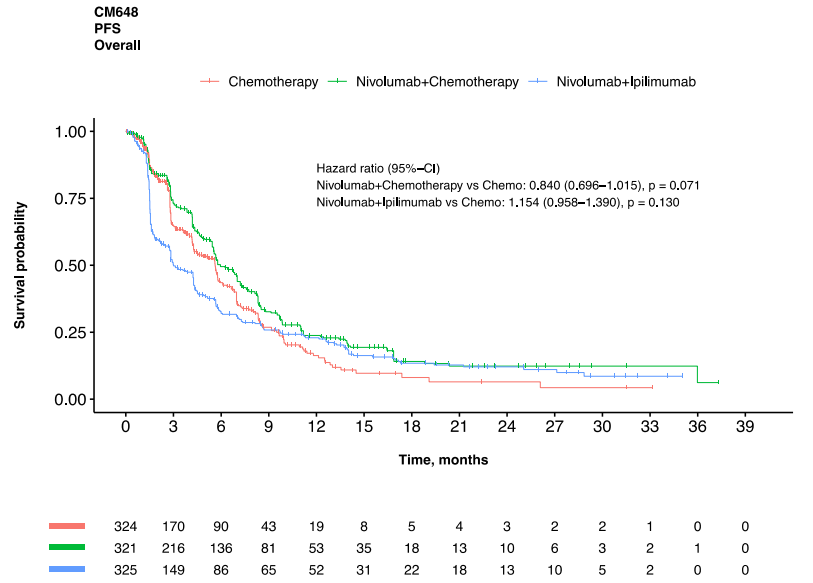
eFigure 3. Comparisons to Original Curves for Overall and PD-L1–High Subgroups

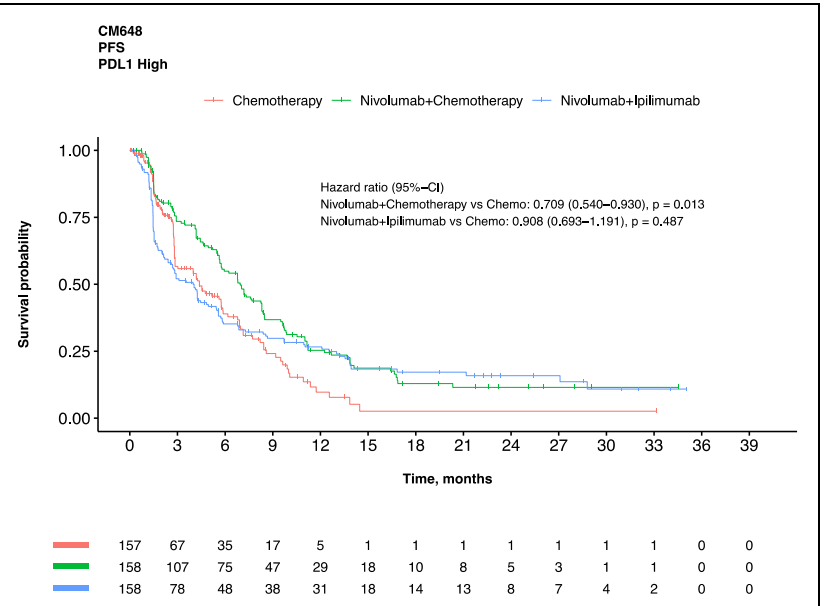
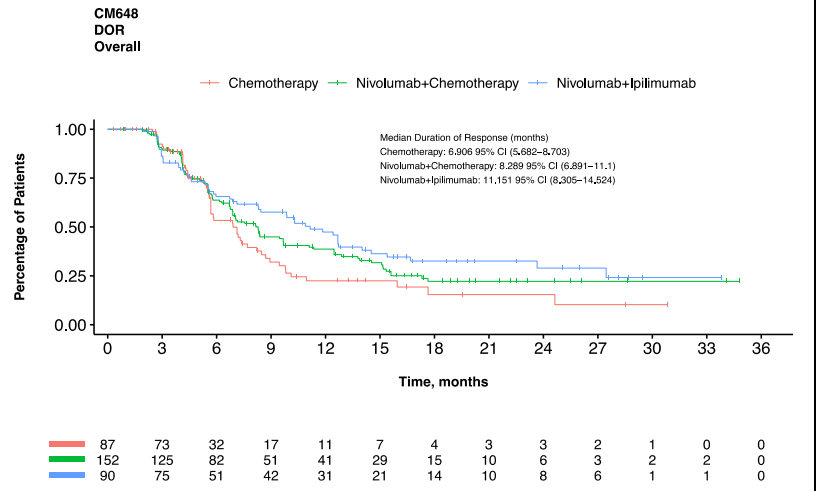
Study, outcome, cohort	Original	Reconstructed
ATTRACTION 3, Overall survival, overall cohort	The original figure may be found in the primary trial manuscript Kato K, Cho BC, Takahashi M, Okada M, Lin CY, Chin K, Kadowaki S, Ahn MJ, Hamamoto Y, Doki Y, Yen CC, Kubota Y, Kim SB, Hsu CH, Holtved E, Xynos I, Kodani M, Kitagawa Y. Nivolumab versus chemotherapy in patients with advanced oesophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2019 Nov;20(11):1506-1517. doi: 10.1016/S1470-2045(19)30626-6. Epub 2019 Sep 30. Erratum in: Lancet Oncol. 2019 Nov;20(11):e613. PMID: 31582355. Figure 2A	

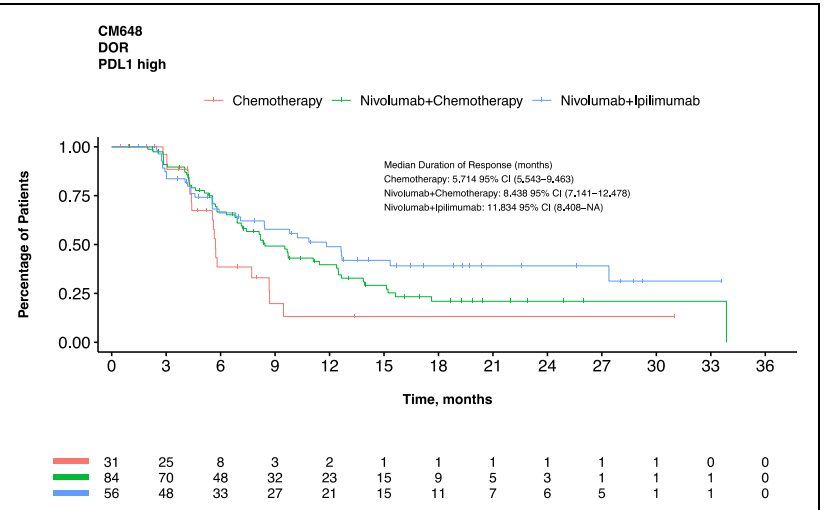
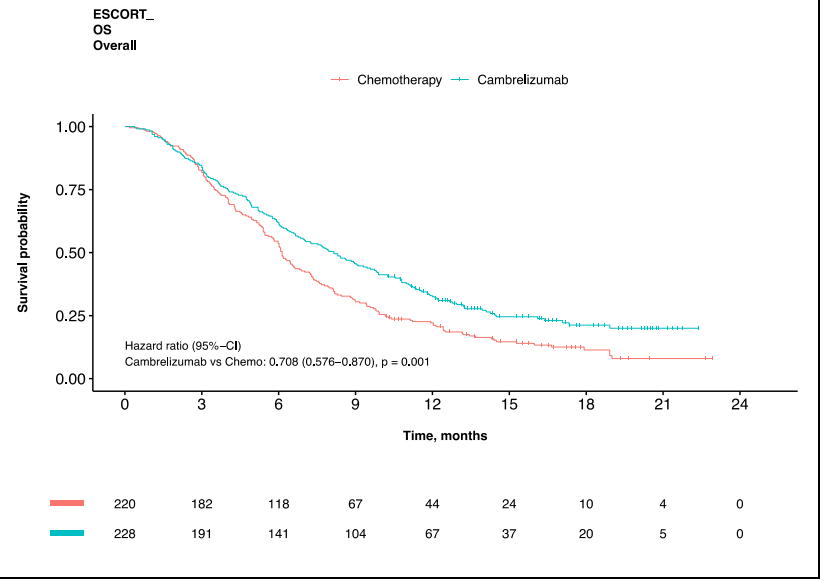
ATTRACTION 3, overall survival, TPS >1%	The original figure may be found in the primary trial manuscript Kato K, Cho BC, Takahashi M, Okada M, Lin CY, Chin K, Kadowaki S, Ahn MJ, Hamamoto Y, Doki Y, Yen CC, Kubota Y, Kim SB, Hsu CH, Holtved E, Xynos I, Kodani M, Kitagawa Y. Nivolumab versus chemotherapy in patients with advanced oesophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2019 Nov;20(11):1506-1517. doi: 10.1016/S1470-2045(19)30626-6. Epub 2019 Sep 30. Erratum in: Lancet Oncol. 2019 Nov;20(11):e613. PMID: 31582355. Figure S2B	

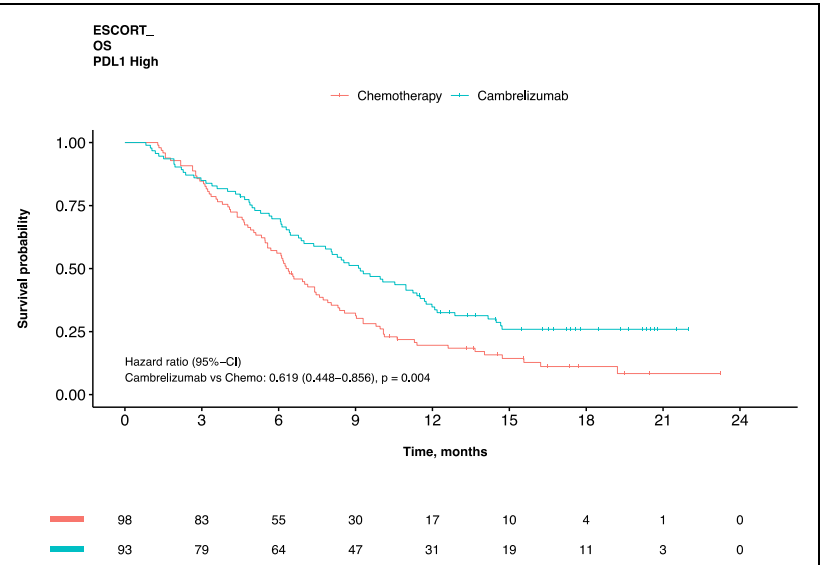
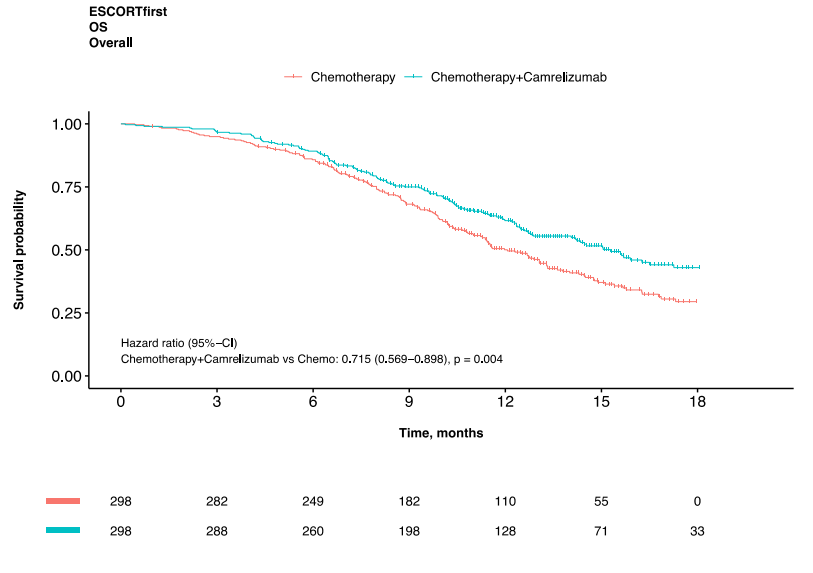
CM648, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, Ogata T, Kawakami H, Hsu CH, Adenis A, El Hajbi F, Di Bartolomeo M, Braghiroli MI, Holtved E, Ostoich SA, Kim HR, Ueno M, Mansoor W, Yang WC, Liu T, Bridgewater J, Makino T, Xynos I, Liu X, Lei M, Kondo K, Patel A, Gricar J, Chau I, Kitagawa Y; CheckMate 648 Trial Investigators. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. N Engl J Med. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380. PMID: 35108470. Figure 1B Figure 2B	

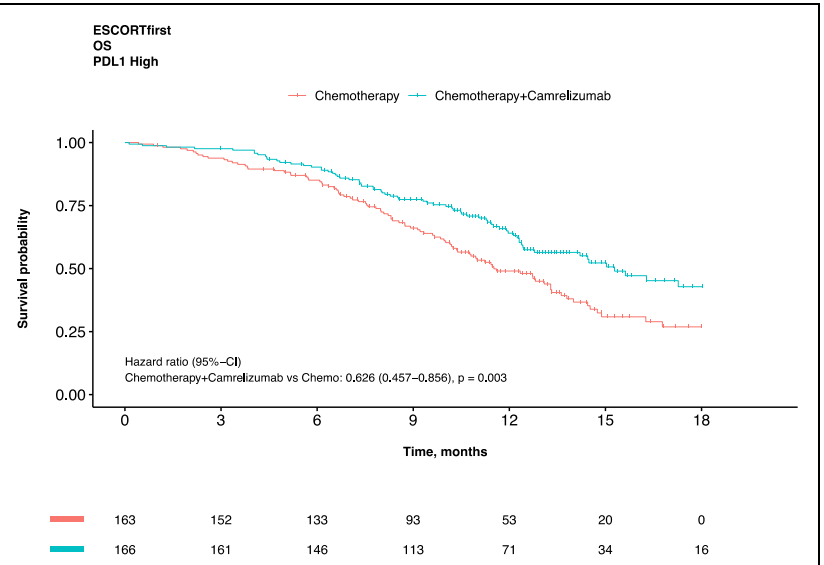
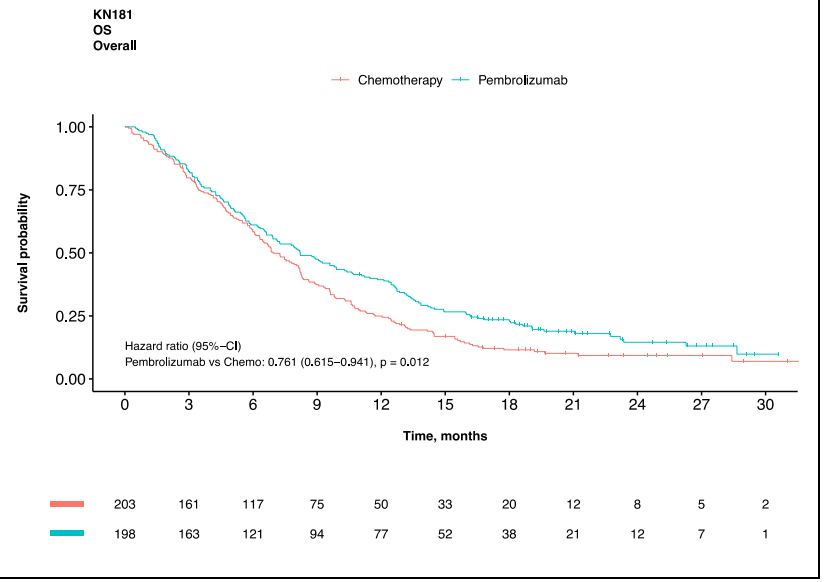
CM648, overall survival, TPS ≥1	The original figure may be found in the primary trial manuscript Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, Ogata T, Kawakami H, Hsu CH, Adenis A, El Hajbi F, Di Bartolomeo M, Braghiroli MI, Holtved E, Ostoich SA, Kim HR, Ueno M, Mansoor W, Yang WC, Liu T, Bridgewater J, Makino T, Xynos I, Liu X, Lei M, Kondo K, Patel A, Gricar J, Chau I, Kitagawa Y; CheckMate 648 Trial Investigators. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. N Engl J Med. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380. PMID: 35108470. Figure 1A Figure 2A	

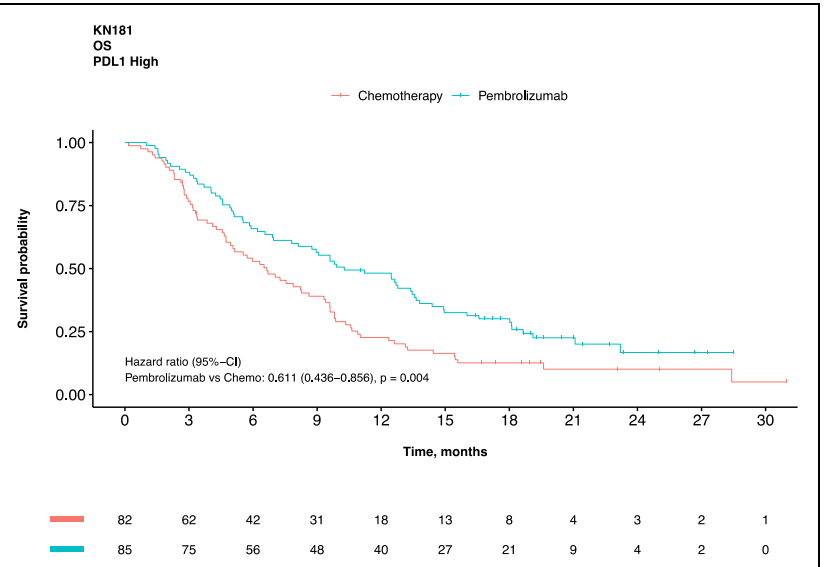
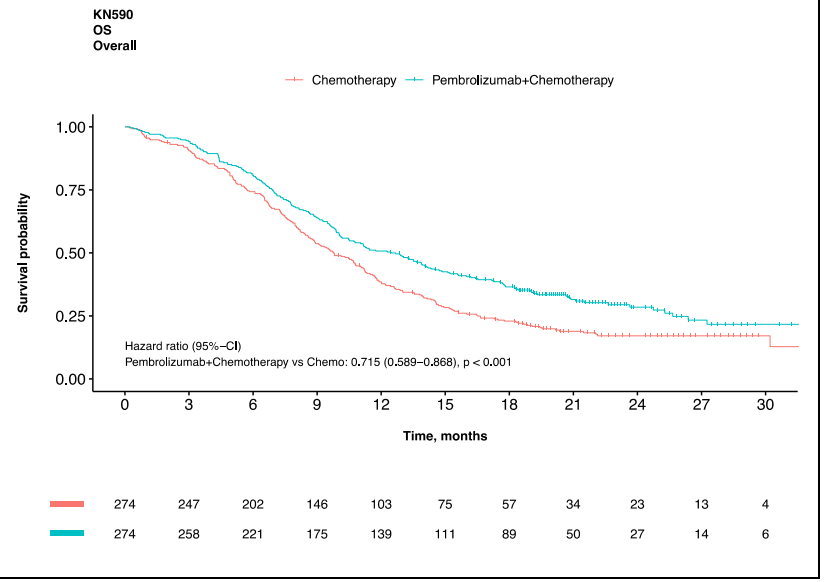
CM648, Progression Free Survival, Overall cohort	The original figure may be found in the primary trial manuscript Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, Ogata T, Kawakami H, Hsu CH, Adenis A, El Hajbi F, Di Bartolomeo M, Braghiroli MI, Holtved E, Ostoich SA, Kim HR, Ueno M, Mansoor W, Yang WC, Liu T, Bridgewater J, Makino T, Xynos I, Liu X, Lei M, Kondo K, Patel A, Gricar J, Chau I, Kitagawa Y; CheckMate 648 Trial Investigators. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. N Engl J Med. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380. PMID: 35108470. Figure 1D Figure 2D	

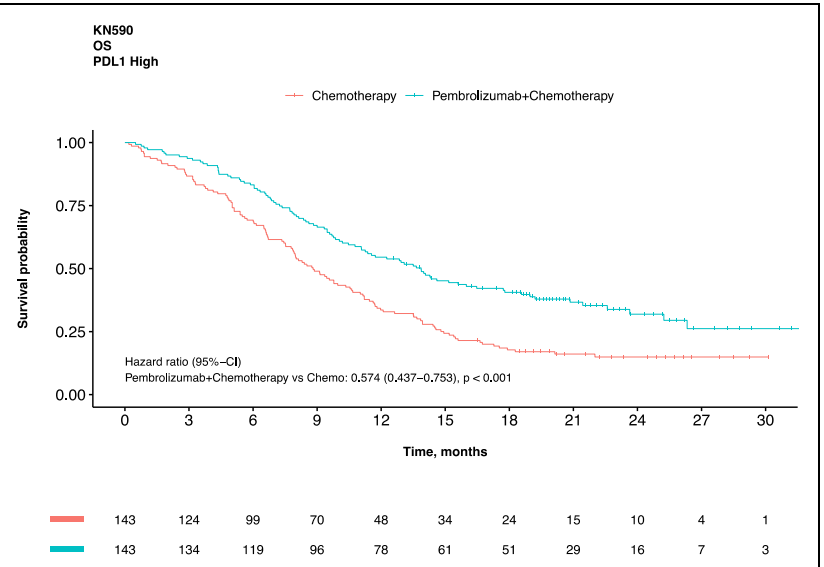
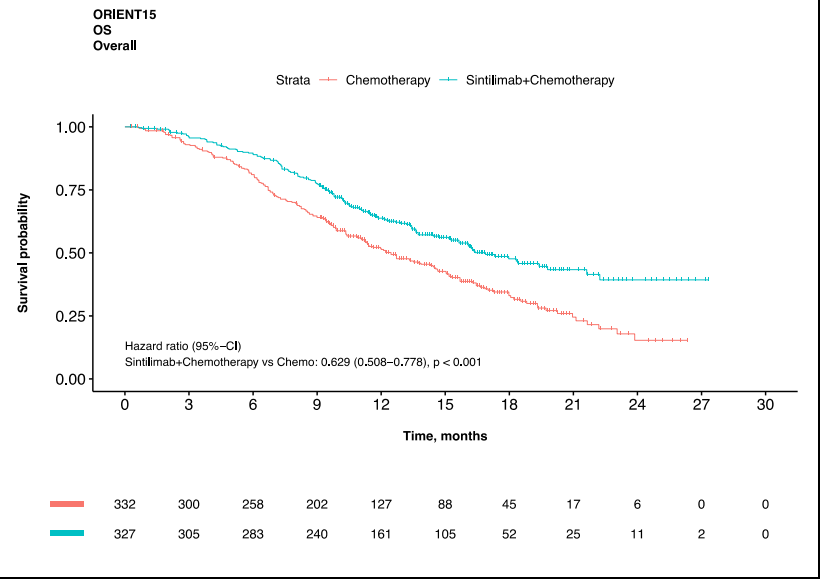
CM648, Progression Free Survival, TPS ≥1	The original figure may be found in the primary trial manuscript Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, Ogata T, Kawakami H, Hsu CH, Adenis A, El Hajbi F, Di Bartolomeo M, Braghiroli MI, Holtved E, Ostoich SA, Kim HR, Ueno M, Mansoor W, Yang WC, Liu T, Bridgewater J, Makino T, Xynos I, Liu X, Lei M, Kondo K, Patel A, Gricar J, Chau I, Kitagawa Y; CheckMate 648 Trial Investigators. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. N Engl J Med. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380. PMID: 35108470. Figure 1C Figure 2C	
CM648, DOR, Overall cohort	The original figure may be found in the primary trial manuscript Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, Ogata T, Kawakami H, Hsu CH, Adenis A, El Hajbi F, Di Bartolomeo M, Braghiroli MI, Holtved E, Ostoich SA, Kim HR, Ueno M, Mansoor W, Yang WC, Liu T, Bridgewater J, Makino T, Xynos I, Liu X, Lei M, Kondo K, Patel A, Gricar J, Chau I, Kitagawa Y; CheckMate 648 Trial Investigators. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. N Engl J Med. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380. PMID: 35108470. Figure S2B Figure S2D	

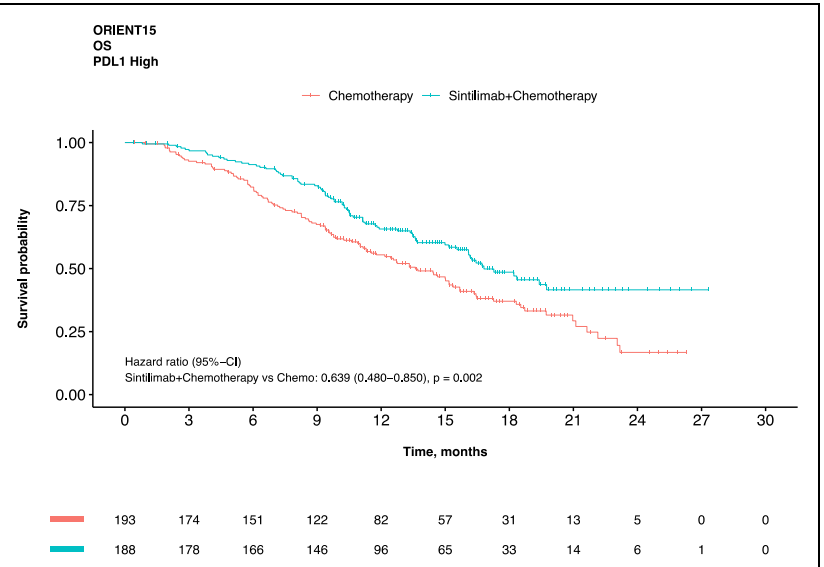
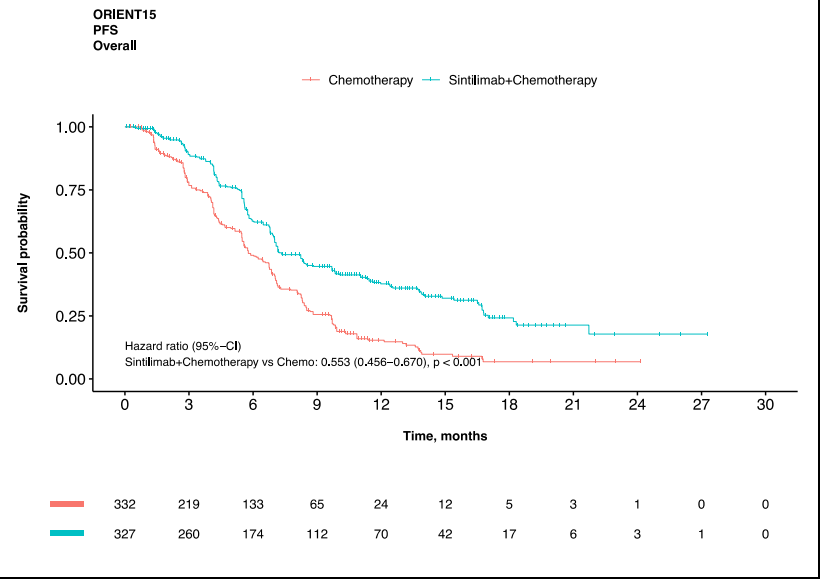
CM648, DOR, TPS ≥1	The original figure may be found in the primary trial manuscript Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, Ogata T, Kawakami H, Hsu CH, Adenis A, El Hajbi F, Di Bartolomeo M, Braghiroli MI, Holtved E, Ostoich SA, Kim HR, Ueno M, Mansoor W, Yang WC, Liu T, Bridgewater J, Makino T, Xynos I, Liu X, Lei M, Kondo K, Patel A, Gricar J, Chau I, Kitagawa Y; CheckMate 648 Trial Investigators. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. N Engl J Med. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380. PMID: 35108470. Figure S2A Figure S2C	
ESCORT, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Huang J, Xu J, Chen Y, Zhuang W, Zhang Y, Chen Z, Chen J, Zhang H, Niu Z, Fan Q, Lin L, Gu K, Liu Y, Ba Y, Miao Z, Jiang X, Zeng M, Chen J, Fu Z, Gan L, Wang J, Zhan X, Liu T, Li Z, Shen L, Shu Y, Zhang T, Yang Q, Zou J; ESCORT Study Group. Camrelizumab versus investigator's choice of chemotherapy as second-line therapy for advanced or metastatic oesophageal squamous cell carcinoma (ESCORT): a multicentre, randomised, open-label, phase 3 study. Lancet Oncol. 2020 Jun;21(6):832-842. doi: 10.1016/S1470-2045(20)30110-8. Epub 2020 May 13. PMID: 32416073. Figure 2A	

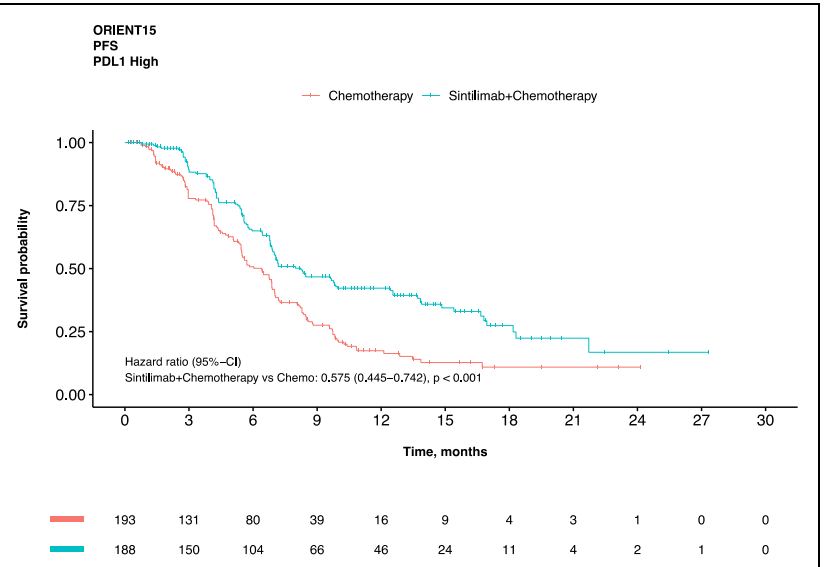
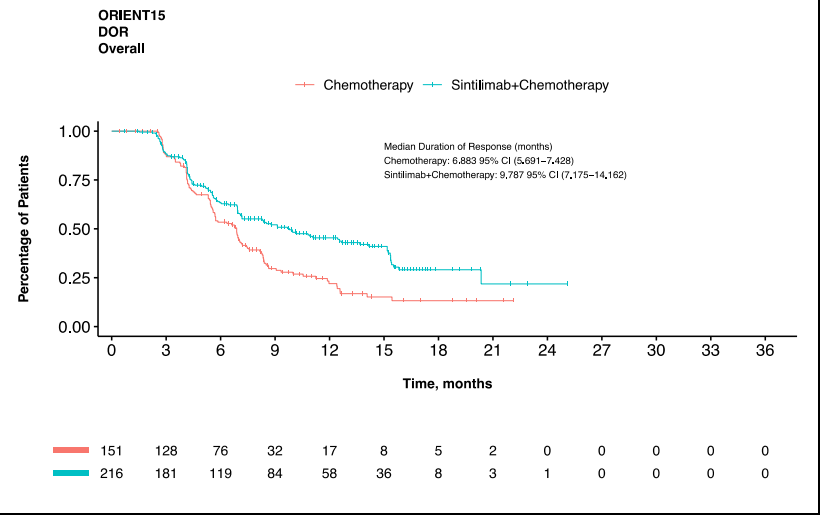
ESCORT, overall survival, TPS≥1	The original figure may be found in the primary trial manuscript Huang J, Xu J, Chen Y, Zhuang W, Zhang Y, Chen Z, Chen J, Zhang H, Niu Z, Fan Q, Lin L, Gu K, Liu Y, Ba Y, Miao Z, Jiang X, Zeng M, Chen J, Fu Z, Gan L, Wang J, Zhan X, Liu T, Li Z, Shen L, Shu Y, Zhang T, Yang Q, Zou J; ESCORT Study Group. Camrelizumab versus investigator's choice of chemotherapy as second-line therapy for advanced or metastatic oesophageal squamous cell carcinoma (ESCORT): a multicentre, randomised, open-label, phase 3 study. Lancet Oncol. 2020 Jun;21(6):832-842. doi: 10.1016/S1470-2045(20)30110-8. Epub 2020 May 13. PMID: 32416073. Figure S3	
ESCORT1, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Luo H, Lu J, Bai Y, Mao T, Wang J, Fan Q, Zhang Y, Zhao K, Chen Z, Gao S, Li J, Fu Z, Gu K, Liu Z, Wu L, Zhang X, Feng J, Niu Z, Ba Y, Zhang H, Liu Y, Zhang L, Min X, Huang J, Cheng Y, Wang D, Shen Y, Yang Q, Zou J, Xu RH; ESCORT-1st Investigators. Effect of Camrelizumab vs Placebo Added to Chemotherapy on Survival and Progression-Free Survival in Patients With Advanced or Metastatic Esophageal Squamous Cell Carcinoma: The ESCORT-1st Randomized Clinical Trial. JAMA. 2021 Sep 14;326(10):916-925. doi: 10.1001/jama.2021.12836. PMID: 34519801; PMCID: PMC8441593. Figure 2A	

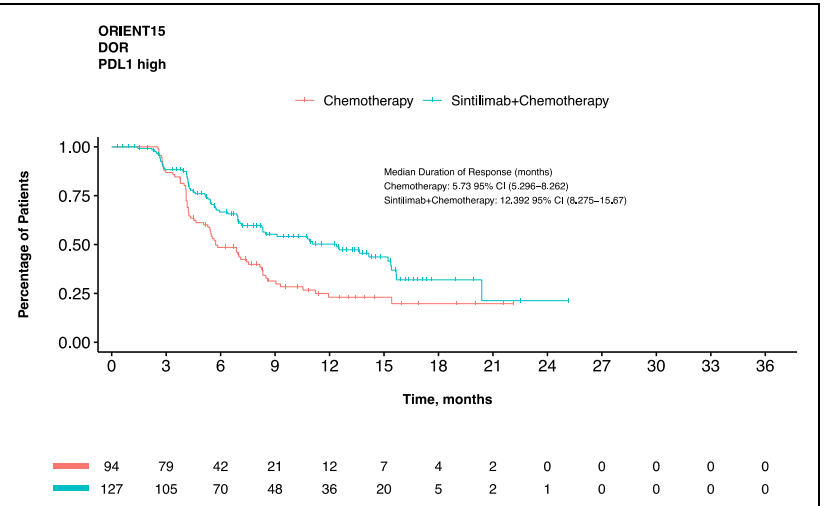
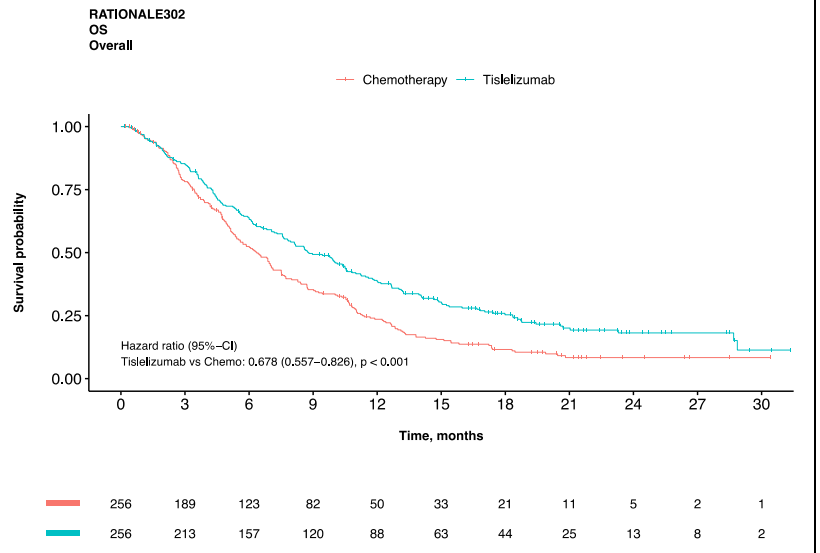
ESCORT1, overall survival, TPS≥1	The original figure may be found in the primary trial manuscript Luo H, Lu J, Bai Y, Mao T, Wang J, Fan Q, Zhang Y, Zhao K, Chen Z, Gao S, Li J, Fu Z, Gu K, Liu Z, Wu L, Zhang X, Feng J, Niu Z, Ba Y, Zhang H, Liu Y, Zhang L, Min X, Huang J, Cheng Y, Wang D, Shen Y, Yang Q, Zou J, Xu RH; ESCORT-1st Investigators. Effect of Camrelizumab vs Placebo Added to Chemotherapy on Survival and Progression-Free Survival in Patients With Advanced or Metastatic Esophageal Squamous Cell Carcinoma: The ESCORT-1st Randomized Clinical Trial. JAMA. 2021 Sep 14;326(10):916-925. doi: 10.1001/jama.2021.12836. PMID: 34519801; PMCID: PMC8441593. eFigure 5B	
KN181, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Kojima T, Shah MA, Muro K, Francois E, Adenis A, Hsu CH, Doi T, Moriwaki T, Kim SB, Lee SH, Bennouna J, Kato K, Shen L, Enzinger P, Qin SK, Ferreira P, Chen J, Girotto G, de la Fouchardiere C, Senellart H, Al-Rajabi R, Lordick F, Wang R, Suryawanshi S, Bhagia P, Kang SP, Metges JP; KEYNOTE-181 Investigators. Randomized Phase III KEYNOTE-181 Study of Pembrolizumab Versus Chemotherapy in Advanced Esophageal Cancer. J Clin Oncol. 2020 Dec 10;38(35):4138-4148. doi: 10.1200/JCO.20.01888. Epub 2020 Oct 7. PMID: 33026938. Figure 2B	

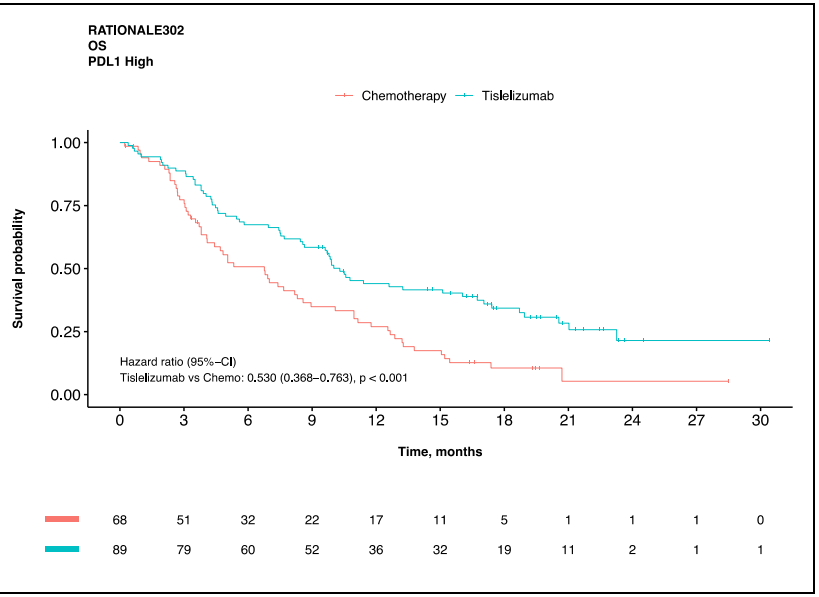
KN181, overall survival, CPS≥10	The original figure may be found in the primary trial manuscript Kojima T, Shah MA, Muro K, Francois E, Adenis A, Hsu CH, Doi T, Moriwaki T, Kim SB, Lee SH, Bennouna J, Kato K, Shen L, Enzinger P, Qin SK, Ferreira P, Chen J, Girotto G, de la Fouchardiere C, Senellart H, Al-Rajabi R, Lordick F, Wang R, Suryawanshi S, Bhagia P, Kang SP, Metges JP; KEYNOTE-181 Investigators. Randomized Phase III KEYNOTE-181 Study of Pembrolizumab Versus Chemotherapy in Advanced Esophageal Cancer. J Clin Oncol. 2020 Dec 10;38(35):4138-4148. doi: 10.1200/JCO.20.01888. Epub 2020 Oct 7. PMID: 33026938. Figure S4	
KN590, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Sun JM, Shen L, Shah MA, Enzinger P, Adenis A, Doi T, Kojima T, Metges JP, Li Z, Kim SB, Cho BC, Mansoor W, Li SH, Sunpaweravong P, Maqueda MA, Goekkurt E, Hara H, Antunes L, Fountzilas C, Tsuji A, Oliden VC, Liu Q, Shah S, Bhagia P, Kato K; KEYNOTE-590 Investigators. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. Lancet. 2021 Aug 28;398(10302):759-771. doi: 10.1016/S0140-6736(21)01234-4. Erratum in: Lancet. 2021 Nov 20;398(10314):1874. PMID: 34454674. Figure 2B	

KN590, overall survival, CPS≥10	The original figure may be found in the primary trial manuscript Sun JM, Shen L, Shah MA, Enzinger P, Adenis A, Doi T, Kojima T, Metges JP, Li Z, Kim SB, Cho BC, Mansoor W, Li SH, Sunpaweravong P, Maqueda MA, Goekkurt E, Hara H, Antunes L, Fountzilas C, Tsuji A, Oliden VC, Liu Q, Shah S, Bhagia P, Kato K; KEYNOTE-590 Investigators. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. Lancet. 2021 Aug 28;398(10302):759-771. doi: 10.1016/S0140-6736(21)01234-4. Erratum in: Lancet. 2021 Nov 20;398(10314):1874. PMID: 34454674. Figure 2A	
ORIENT15, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Lu Z, Wang J, Shu Y, Liu L, Kong L, Yang L, Wang B, Sun G, Ji Y, Cao G, Liu H, Cui T, Li N, Qiu W, Li G, Hou X, Luo H, Xue L, Zhang Y, Yue W, Liu Z, Wang X, Gao S, Pan Y, Galais MP, Zaanan A, Ma Z, Li H, Wang Y, Shen L; ORIENT-15 study group. Sintilimab versus placebo in combination with chemotherapy as first line treatment for locally advanced or metastatic oesophageal squamous cell carcinoma (ORIENT-15): multicentre, randomised, double blind, phase 3 trial. BMJ. 2022 Apr 19;377:e068714. doi: 10.1136/bmj-2021-068714. PMID: 35440464; PMCID: PMC9016493. Figure 2 (top)	

ORIENT15, overall survival, CPS≥10	The original figure may be found in the primary trial manuscript Lu Z, Wang J, Shu Y, Liu L, Kong L, Yang L, Wang B, Sun G, Ji Y, Cao G, Liu H, Cui T, Li N, Qiu W, Li G, Hou X, Luo H, Xue L, Zhang Y, Yue W, Liu Z, Wang X, Gao S, Pan Y, Galais MP, Zaanan A, Ma Z, Li H, Wang Y, Shen L; ORIENT-15 study group. Sintilimab versus placebo in combination with chemotherapy as first line treatment for locally advanced or metastatic oesophageal squamous cell carcinoma (ORIENT-15): multicentre, randomised, double blind, phase 3 trial. BMJ. 2022 Apr 19;377:e068714. doi: 10.1136/bmj-2021-068714. PMID: 35440464; PMCID: PMC9016493. Figure 2 (bottom)	
ORIENT15, Progression Free Survival, Overall cohort	The original figure may be found in the primary trial manuscript Lu Z, Wang J, Shu Y, Liu L, Kong L, Yang L, Wang B, Sun G, Ji Y, Cao G, Liu H, Cui T, Li N, Qiu W, Li G, Hou X, Luo H, Xue L, Zhang Y, Yue W, Liu Z, Wang X, Gao S, Pan Y, Galais MP, Zaanan A, Ma Z, Li H, Wang Y, Shen L; ORIENT-15 study group. Sintilimab versus placebo in combination with chemotherapy as first line treatment for locally advanced or metastatic oesophageal squamous cell carcinoma (ORIENT-15): multicentre, randomised, double blind, phase 3 trial. BMJ. 2022 Apr 19;377:e068714. doi: 10.1136/bmj-2021-068714. PMID: 35440464; PMCID: PMC9016493. Figure 4 (top)	

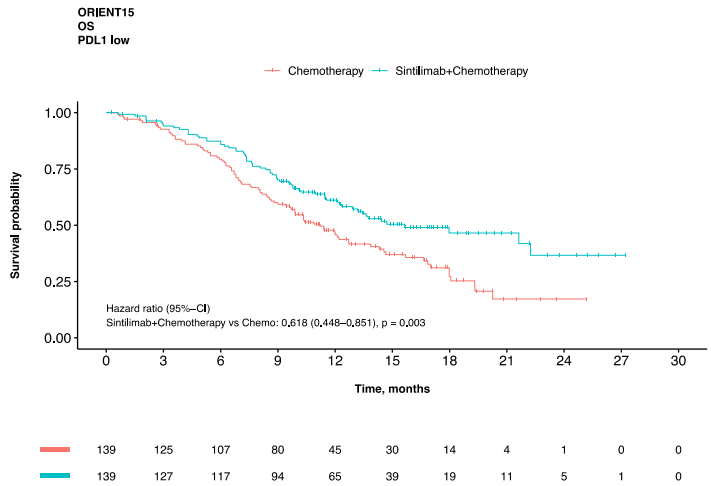
ORIENT15, Progression Free Survival, TPS ≥1	The original figure may be found in the primary trial manuscript Lu Z, Wang J, Shu Y, Liu L, Kong L, Yang L, Wang B, Sun G, Ji Y, Cao G, Liu H, Cui T, Li N, Qiu W, Li G, Hou X, Luo H, Xue L, Zhang Y, Yue W, Liu Z, Wang X, Gao S, Pan Y, Galais MP, Zaanan A, Ma Z, Li H, Wang Y, Shen L; ORIENT-15 study group. Sintilimab versus placebo in combination with chemotherapy as first line treatment for locally advanced or metastatic oesophageal squamous cell carcinoma (ORIENT-15): multicentre, randomised, double blind, phase 3 trial. BMJ. 2022 Apr 19;377:e068714. doi: 10.1136/bmj-2021-068714. PMID: 35440464; PMCID: PMC9016493. Figure 4 (bottom)	
ORIENT15, DOR, Overall cohort	The original figure may be found in the primary trial manuscript Lu Z, Wang J, Shu Y, Liu L, Kong L, Yang L, Wang B, Sun G, Ji Y, Cao G, Liu H, Cui T, Li N, Qiu W, Li G, Hou X, Luo H, Xue L, Zhang Y, Yue W, Liu Z, Wang X, Gao S, Pan Y, Galais MP, Zaanan A, Ma Z, Li H, Wang Y, Shen L; ORIENT-15 study group. Sintilimab versus placebo in combination with chemotherapy as first line treatment for locally advanced or metastatic oesophageal squamous cell carcinoma (ORIENT-15): multicentre, randomised, double blind, phase 3 trial. BMJ. 2022 Apr 19;377:e068714. doi: 10.1136/bmj-2021-068714. PMID: 35440464; PMCID: PMC9016493. Figure S2	

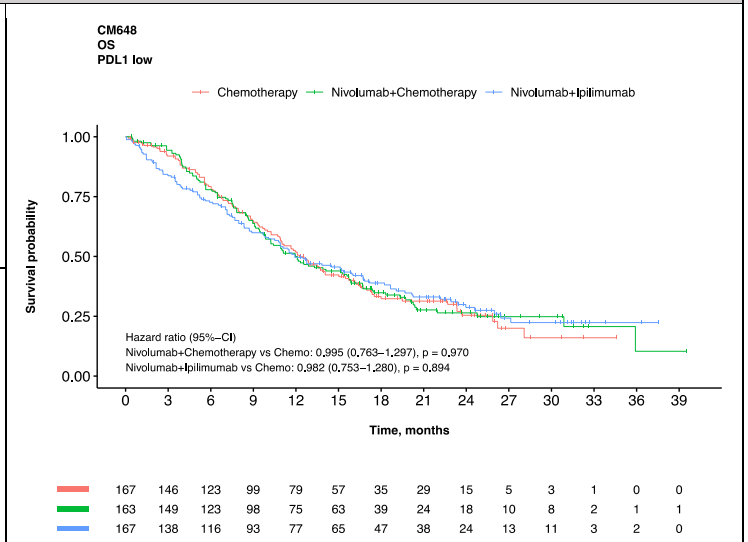
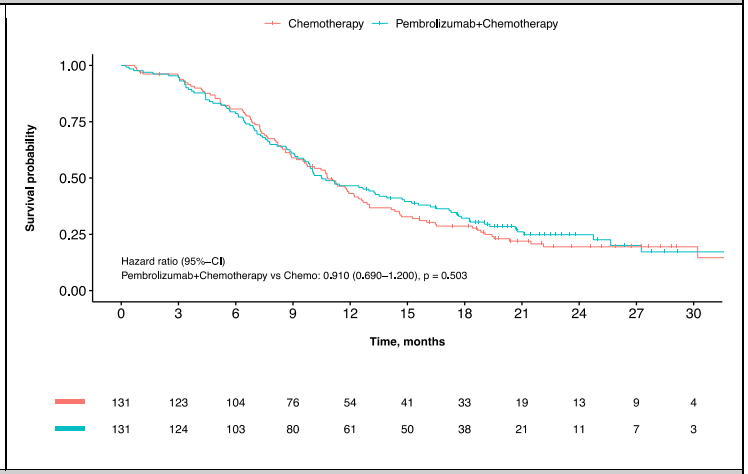
ORIENT15, DOR, TPS ≥1	The original figure may be found in the primary trial manuscript Lu Z, Wang J, Shu Y, Liu L, Kong L, Yang L, Wang B, Sun G, Ji Y, Cao G, Liu H, Cui T, Li N, Qiu W, Li G, Hou X, Luo H, Xue L, Zhang Y, Yue W, Liu Z, Wang X, Gao S, Pan Y, Galais MP, Zaanan A, Ma Z, Li H, Wang Y, Shen L; ORIENT-15 study group. Sintilimab versus placebo in combination with chemotherapy as first line treatment for locally advanced or metastatic oesophageal squamous cell carcinoma (ORIENT-15): multicentre, randomised, double blind, phase 3 trial. BMJ. 2022 Apr 19;377:e068714. doi: 10.1136/bmj-2021-068714. PMID: 35440464; PMCID: PMC9016493. Figure S3	
RATIONALE302, overall survival, overall cohort	The original figure may be found in the primary trial manuscript Shen L, Kato K, Kim SB, Ajani JA, Zhao K, He Z, Yu X, Shu Y, Luo Q, Wang J, Chen Z, Niu Z, Zhang L, Yi T, Sun JM, Chen J, Yu G, Lin CY, Hara H, Bi Q, Satoh T, Pazo-Cid R, Arkenau HT, Borg C, Lordick F, Li L, Ding N, Tao A, Shi J, Van Cutsem E; RATIONALE-302 Investigators. Tislelizumab Versus Chemotherapy as Second-Line Treatment for Advanced or Metastatic Esophageal Squamous Cell Carcinoma (RATIONALE-302): A Randomized Phase III Study. J Clin Oncol. 2022 Sep 10;40(26):3065-3076. doi: 10.1200/JCO.21.01926. Epub 2022 Apr 20. PMID: 35442766; PMCID: PMC9462531. Figure 2A	

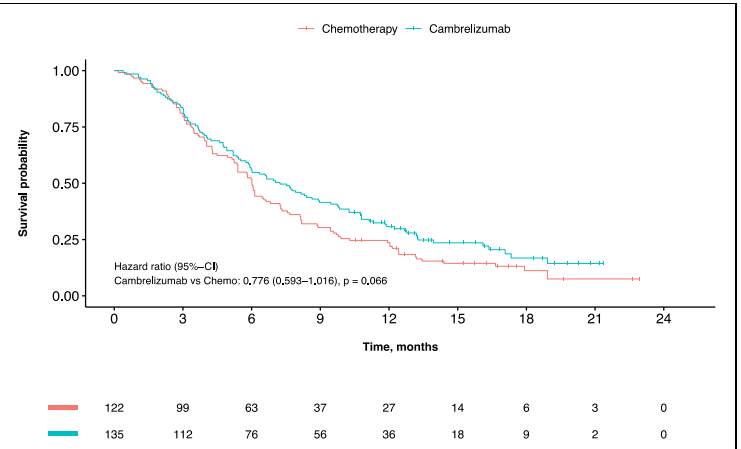
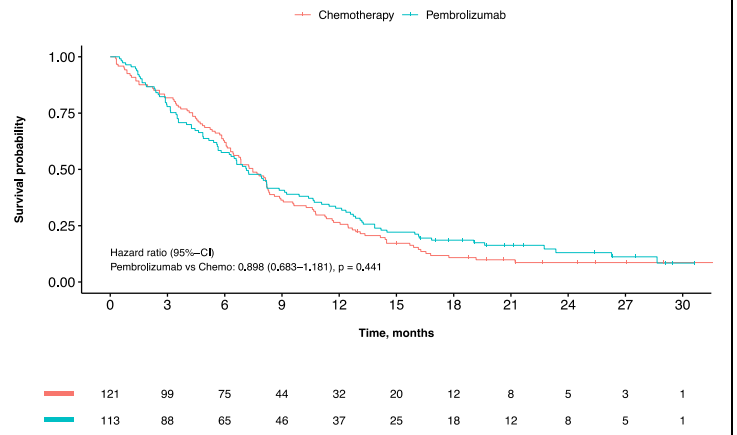
RATIONALE302, overall survival, TAP≥10	The original figure may be found in the primary trial manuscript Shen L, Kato K, Kim SB, Ajani JA, Zhao K, He Z, Yu X, Shu Y, Luo Q, Wang J, Chen Z, Niu Z, Zhang L, Yi T, Sun JM, Chen J, Yu G, Lin CY, Hara H, Bi Q, Satoh T, Pazo-Cid R, Arkenau HT, Borg C, Lordick F, Li L, Ding N, Tao A, Shi J, Van Cutsem E; RATIONALE-302 Investigators. Tislelizumab Versus Chemotherapy as Second-Line Treatment for Advanced or Metastatic Esophageal Squamous Cell Carcinoma (RATIONALE-302): A Randomized Phase III Study. J Clin Oncol. 2022 Sep 10;40(26):3065-3076. doi: 10.1200/JCO.21.01926. Epub 2022 Apr 20. PMID: 35442766; PMCID: PMC9462531. Figure 2B	

Abbreviations: CPS, combined positive score; TPS, tumor proportion score; Chemo, chemotherapy; Immuno, immunotherapy; Nivo, nivolumab; Ipi, ipilimumab; Camre, camrelizumab; Pembro, pembrolizumab; Sinti, sintilimab; Tisle, Tislelizumab; HR, hazard ratio; CI, confidence interval; PD-L1, programmed death ligand 1

eFigure 4. Example Comparisons of KMSubtraction Outcomes With Reported HRs for PD-L1–Low Subgroups

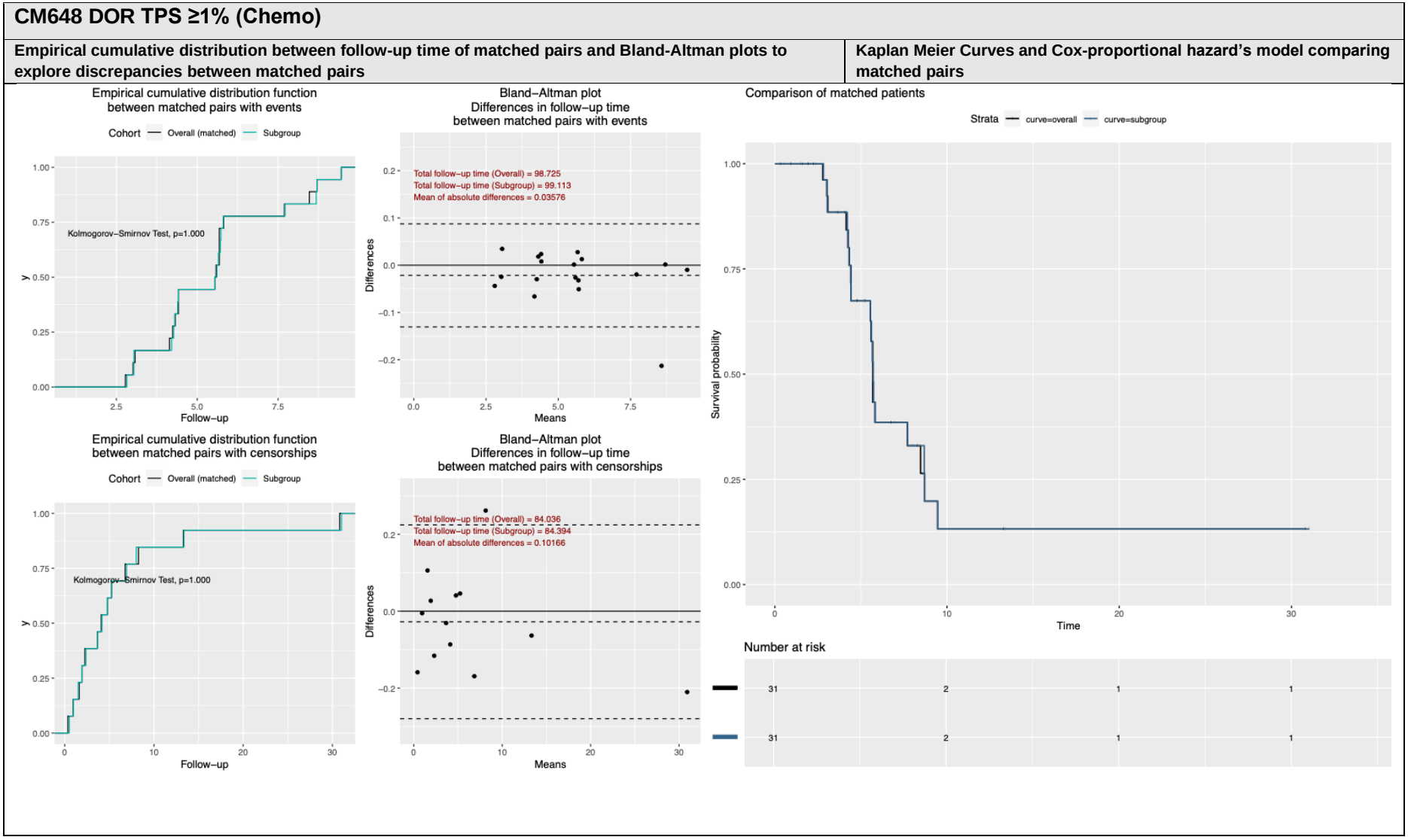
Trial, comparison	PD-L1 expression subgroup	Outcome	Reported		KMSubtraction with bipartite matching
			Hazard ratio (95%-CI)	p-value	Curve, hazard ratio (95%-CI)
ORIENT15 *(Esophageal squamous cell carcinoma)*					
Sintilimab + Chemothrapy (139) vs Chemotherapy (139)	CPS < 10	OS	0.62 (0.45-0.85)	NR	

Checkmate-648 *(Esophageal squamous cell carcinoma)*					
Nivo+Chemo vs Chemo	TPS <1	OS	0.98 (0.76-1.28)	NR	
Nivo+Ipi vs Chemo	TPS <1	OS	0.96 (0.74-1.25)	NR	
KN590					
Pembro + Chemo vs Chemo	CPS < 10	OS	0.99 (0.74-1.32)	HR	
ESCORT					

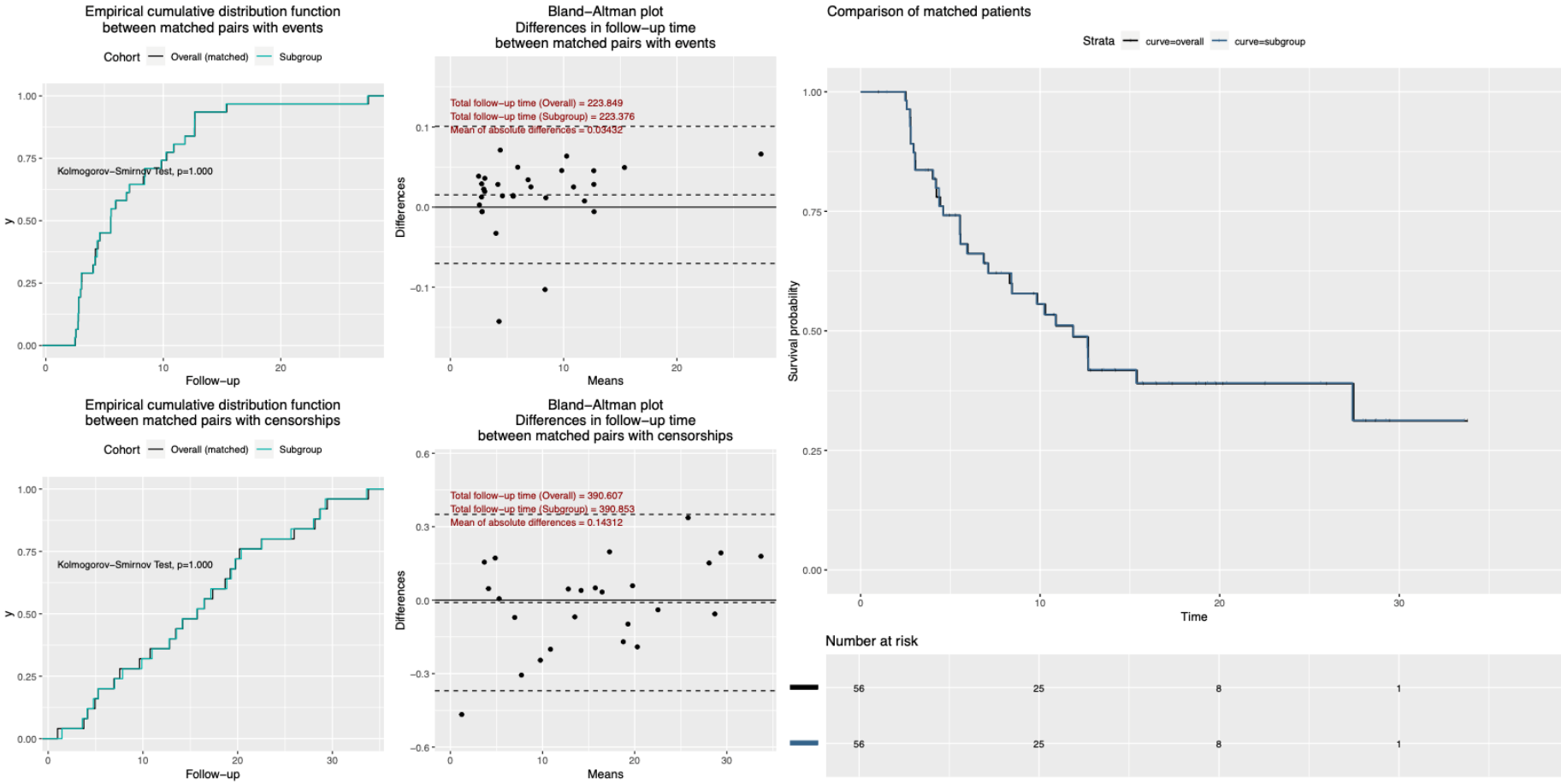
Camre vs Chemo	TPS <1	OS	0.82 (0.62-1.09)	NR	
KN181					
Pembro vs Chemo	CPS <10	OS	0.88 (0.66-1.16)		

Abbreviations: Sinti, Sintilimab; Nivo, nivolumab; Ipi, ipilimumab; Pembro, Pembrolizumab; Chemo, chemotherapy; CI, confidence interval; PD-L1, programmed death ligand 1 ESCC, esophageal squamous cell carcinoma; NR, not reported; TPS, tumor proportion score.

eFigure 5. Evaluation of KMSubtraction Bipartite Matching

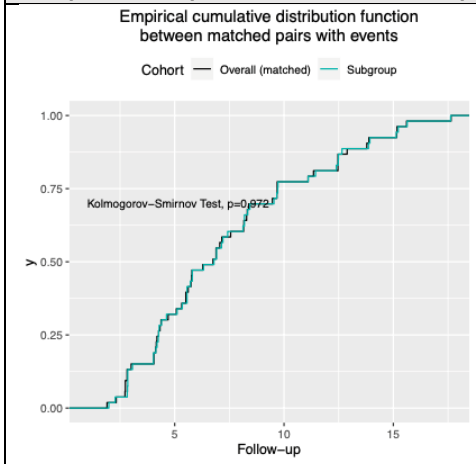


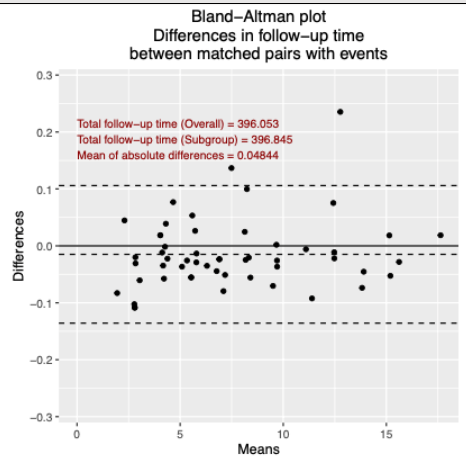
CM648 DOR TPS ≥1% (Nivo + Ipi)	
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	**Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs**

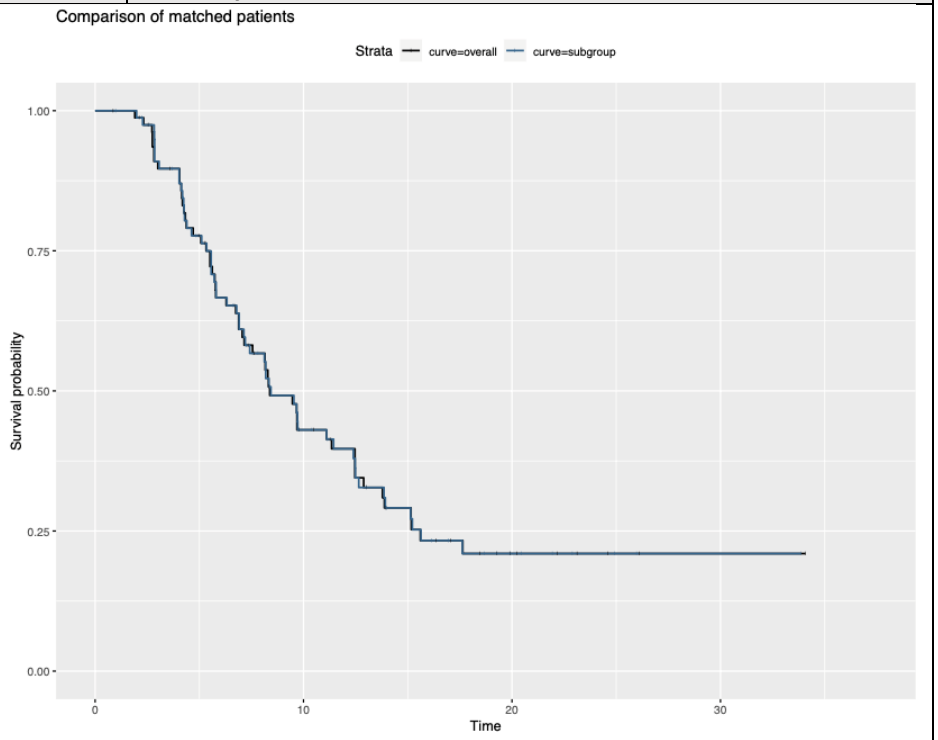


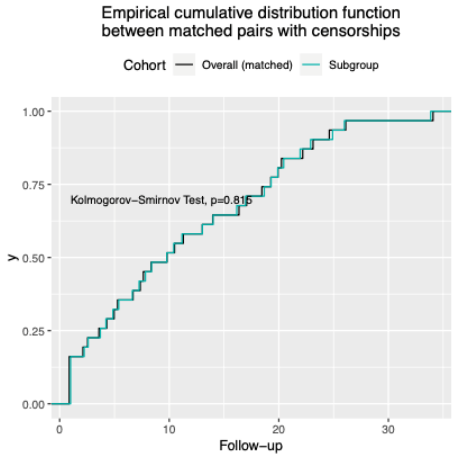
CM648 DOR TPS ≥1% (Nivo + Chemo)

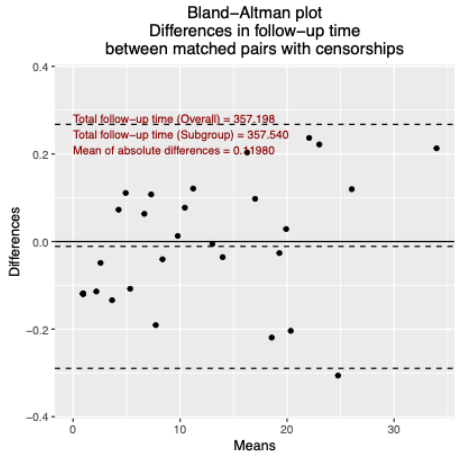
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs





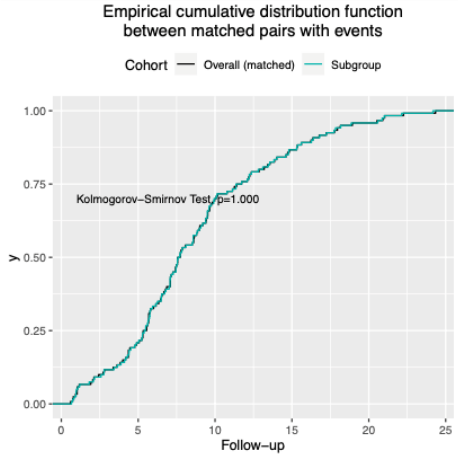


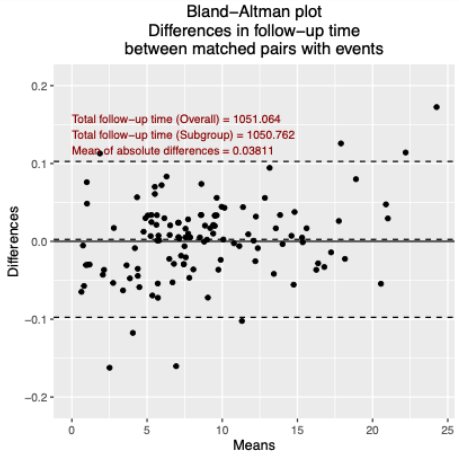


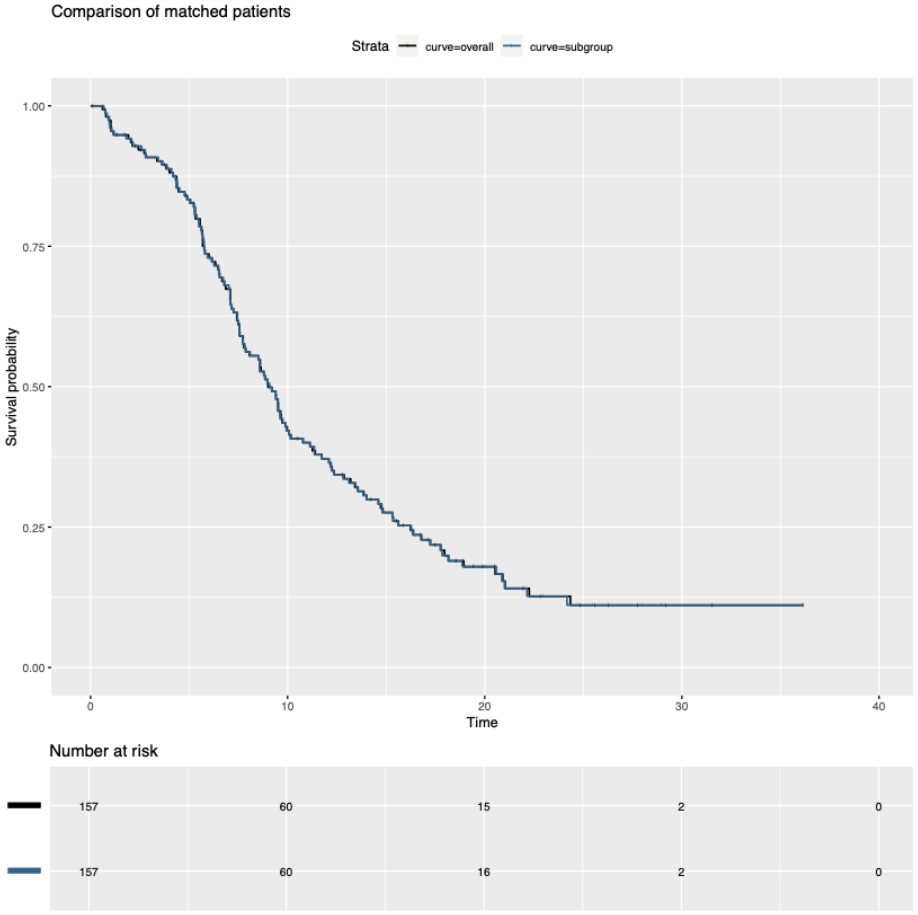


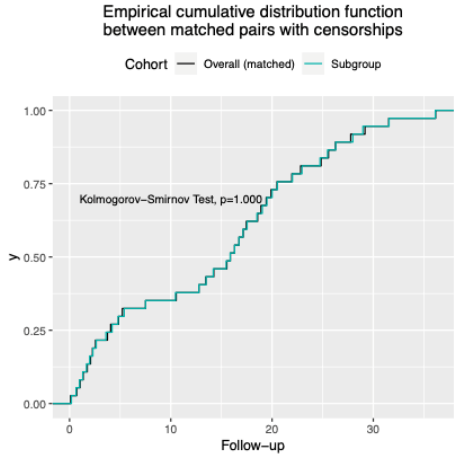
CM648 OS TPS ≥1% (Chemo)

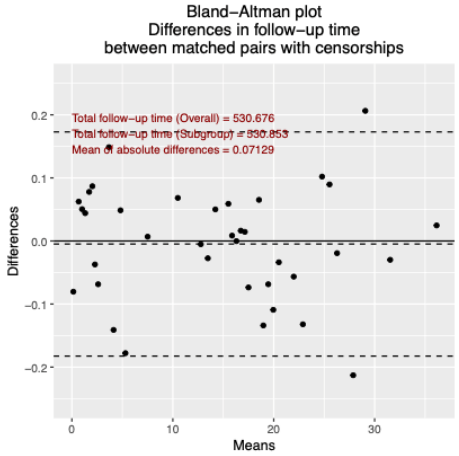
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs





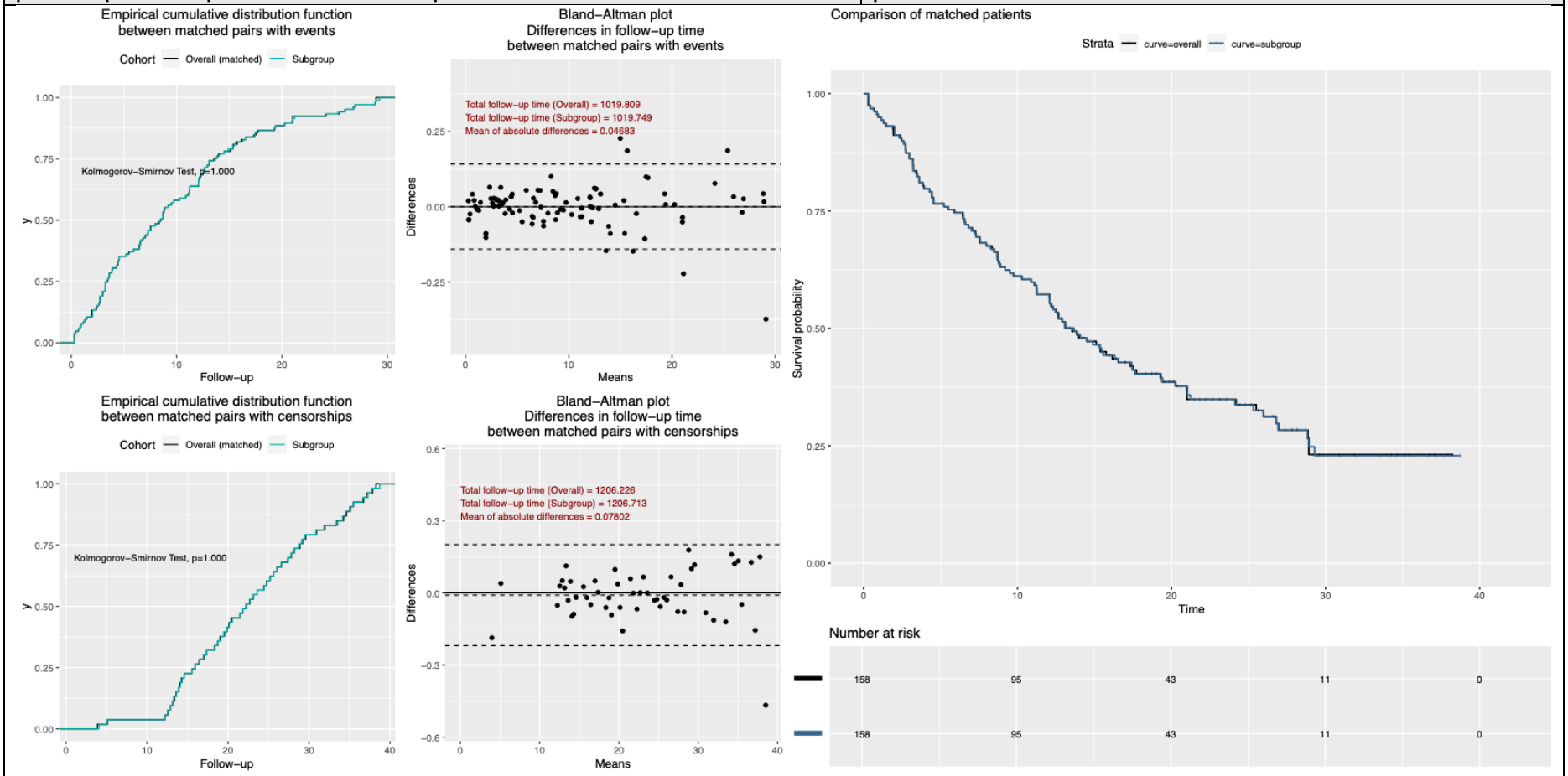






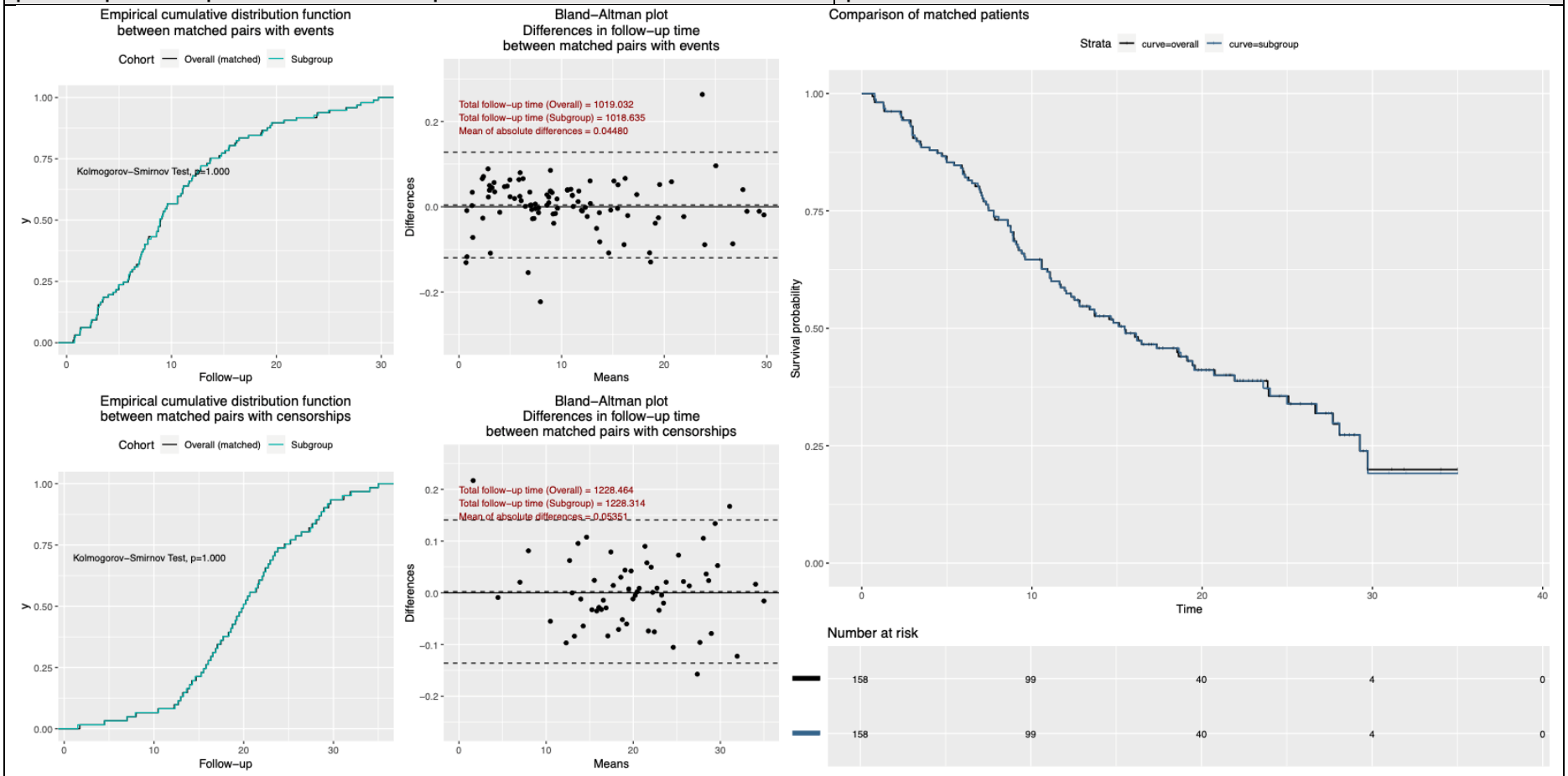
CM648 OS TPS ≥1% (Nivo + Ipi)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs



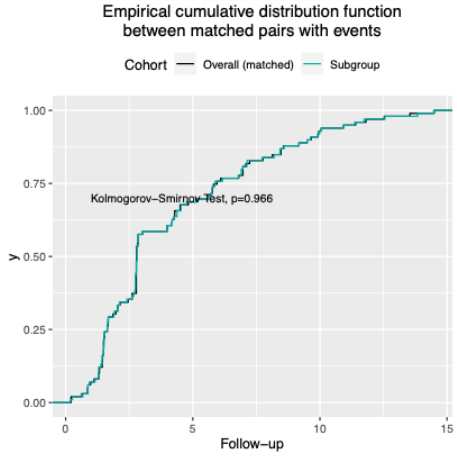
CM648 OS TPS ≥1% (Nivo + Chemo)

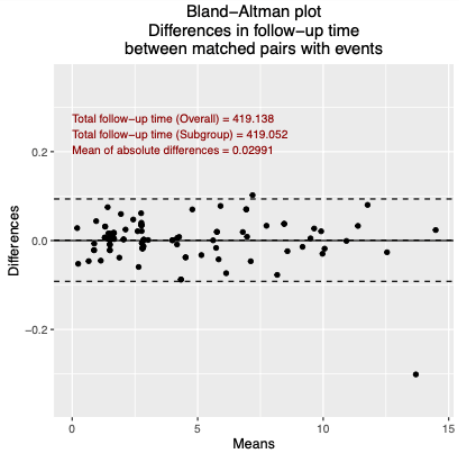
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

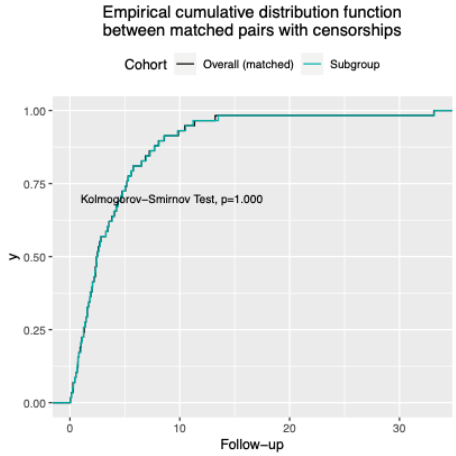


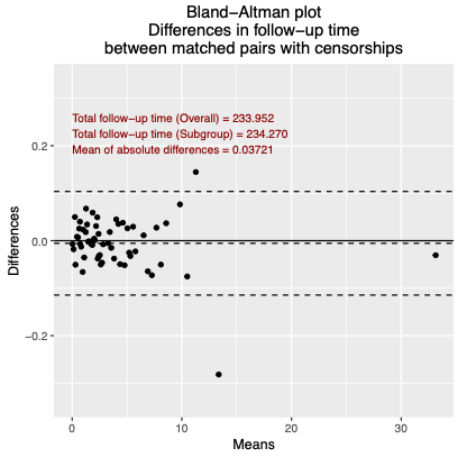
CM648 PFS TPS ≥1% (Chemo)

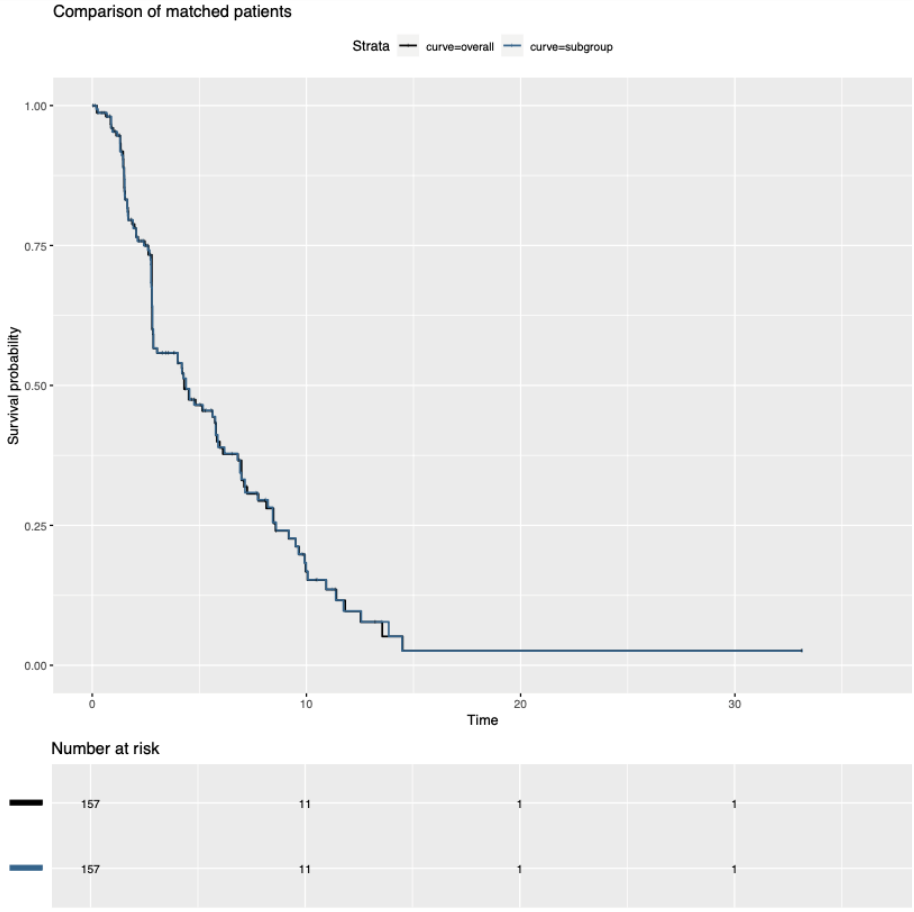
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs







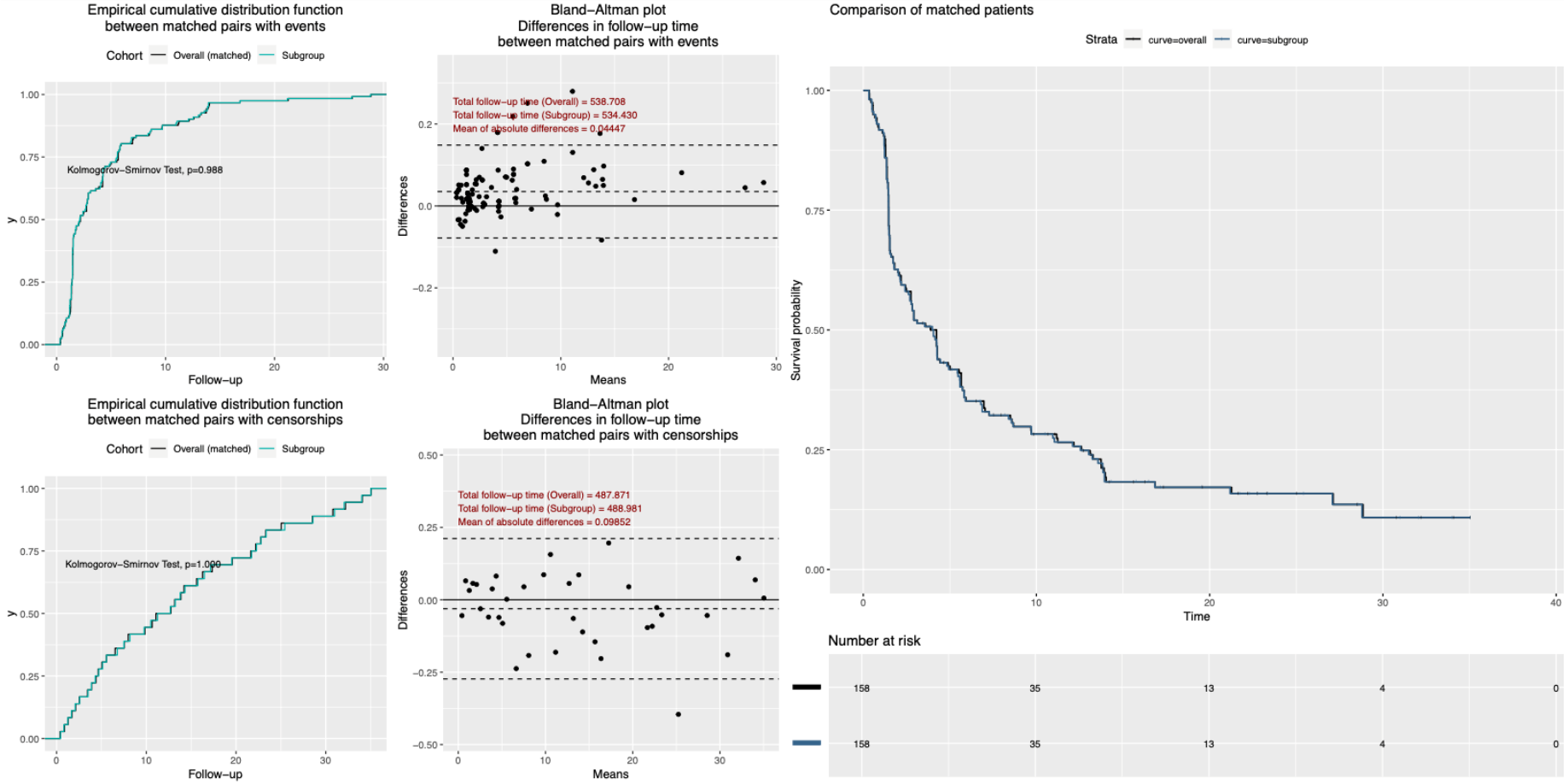




CM648 PFS TPS ≥1% (Nivo + Ipi)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

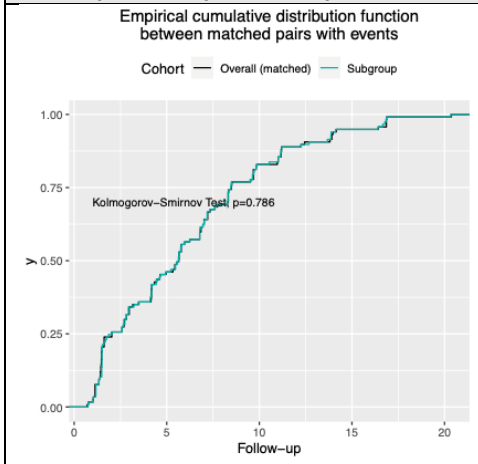
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

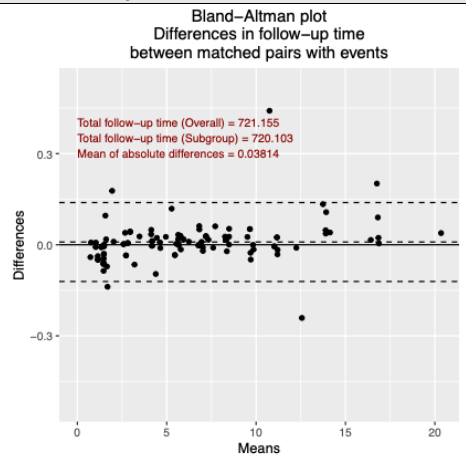


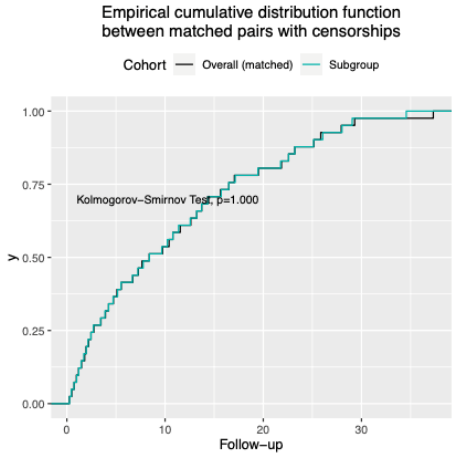
CM648 PFS TPS ≥1% (Nivo + Chemo)

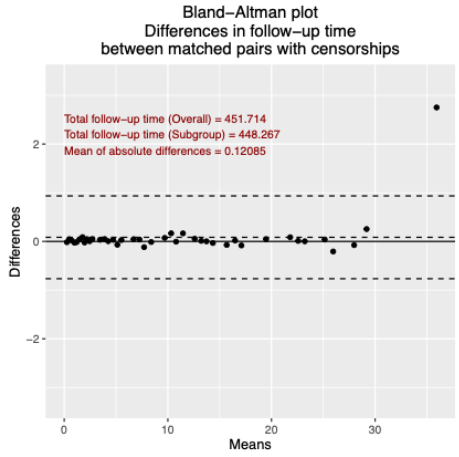
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

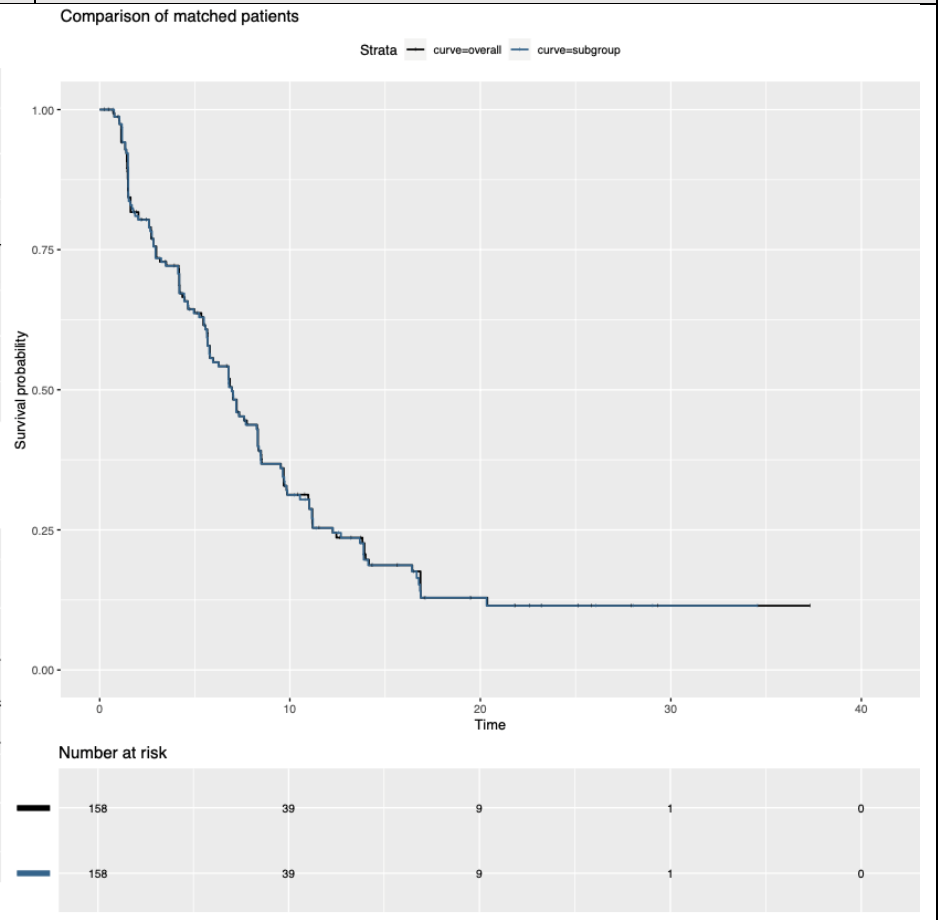
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs





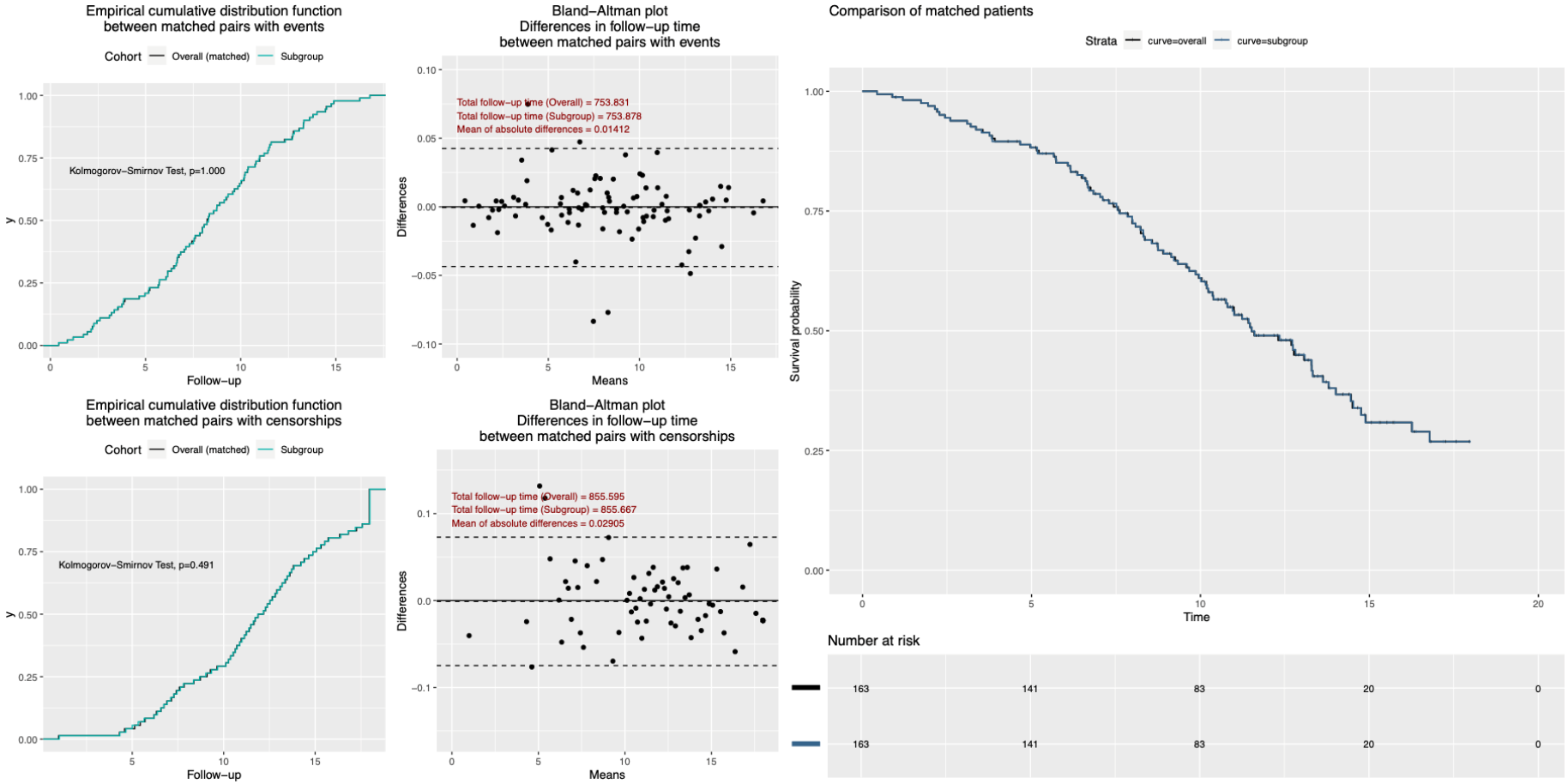






ESCORT1st OS TPS ≥1% (Chemo)

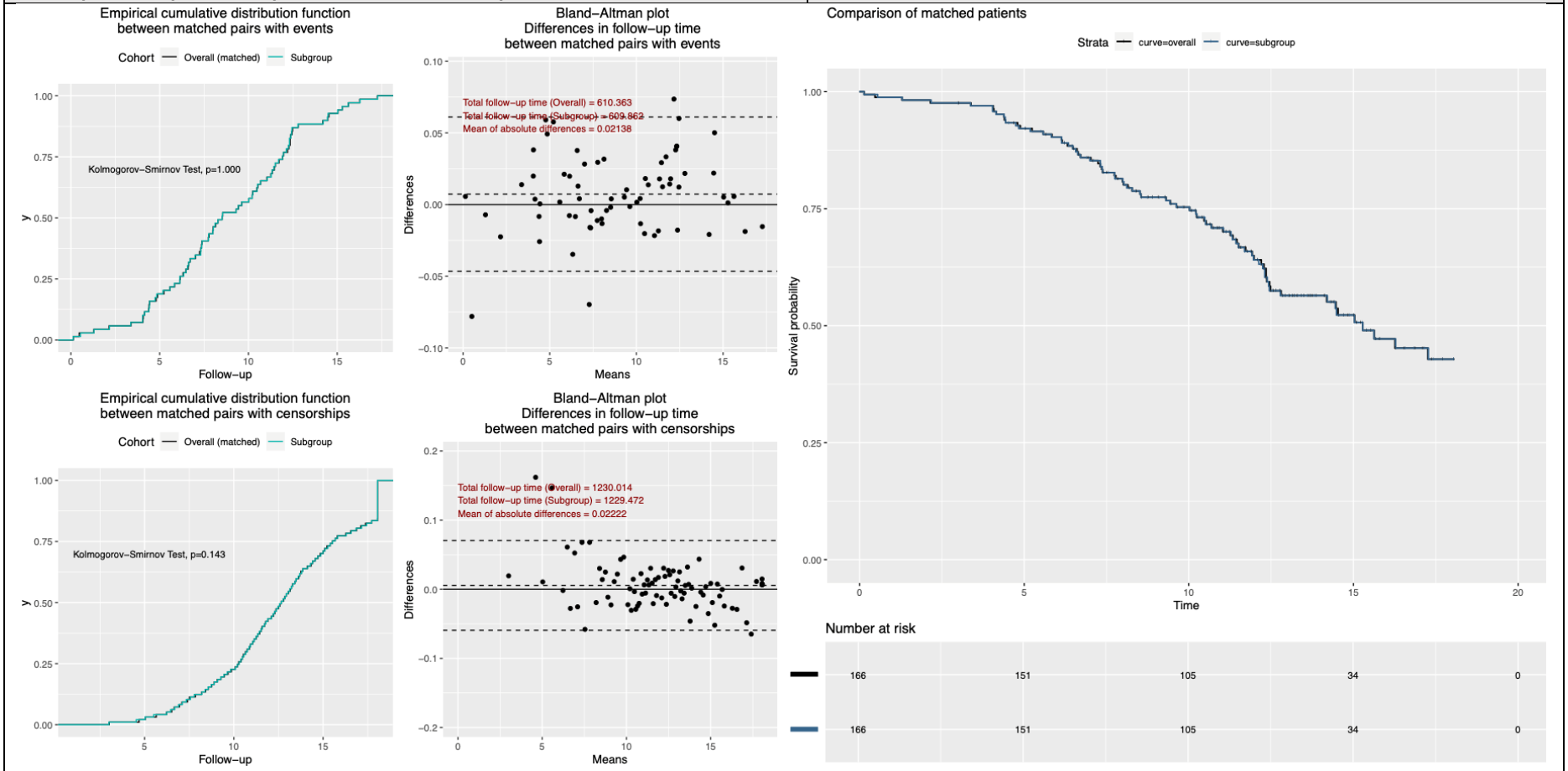
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs



ESCORT1st OS TPS ≥1% (Camre + Chemo)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

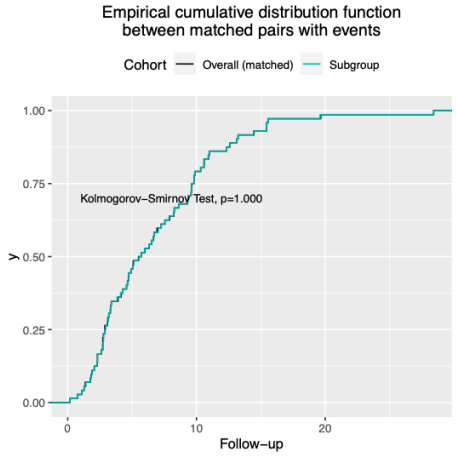
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

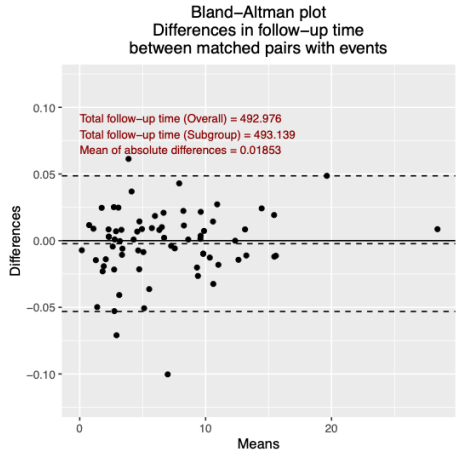


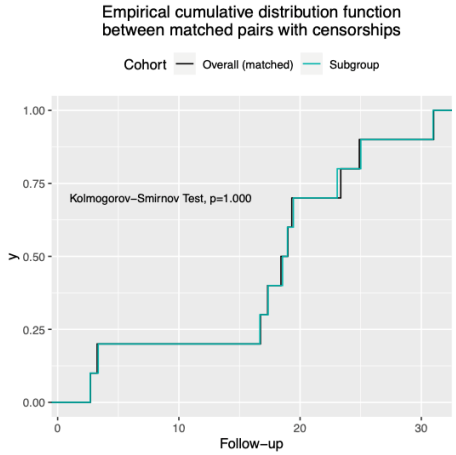
KN181 OS CPS ≥10% (Chemo)

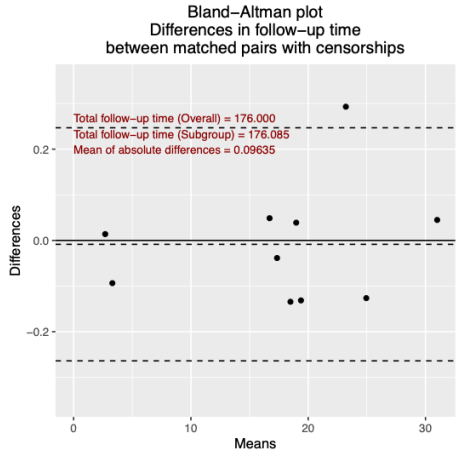
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

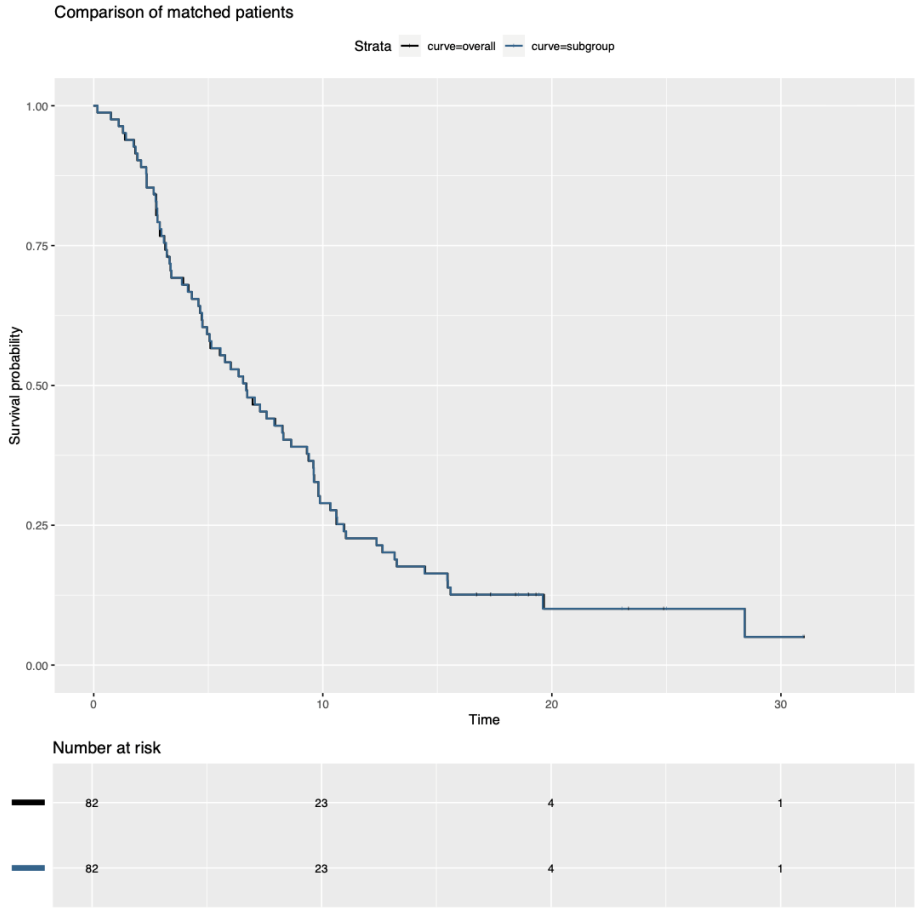
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs







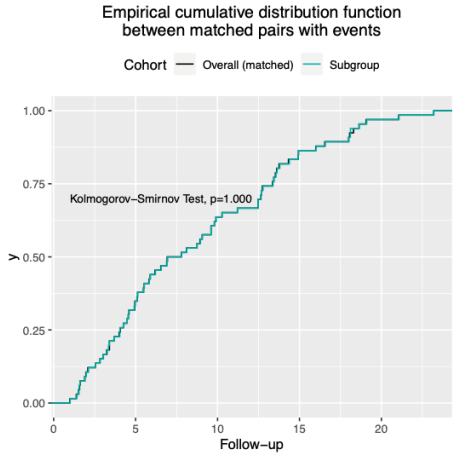


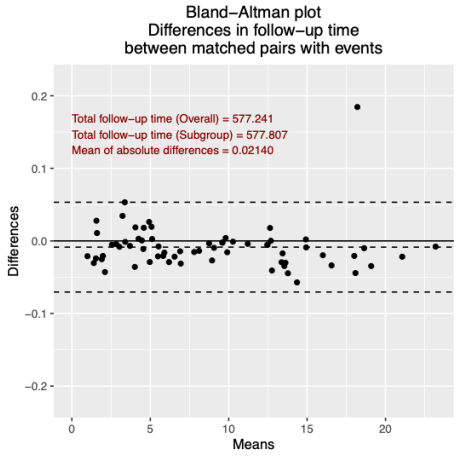


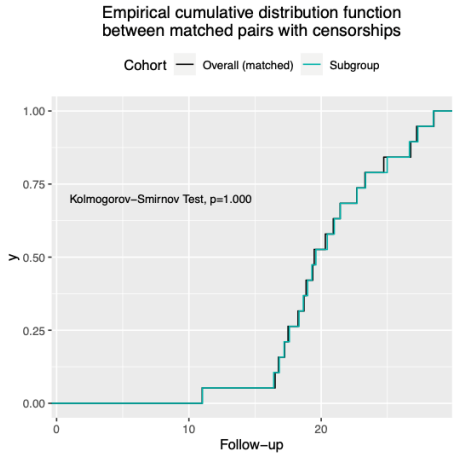
KN181 OS CPS ≥10% (Pembro)

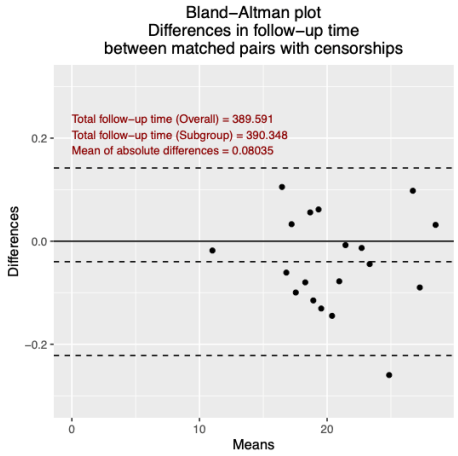
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

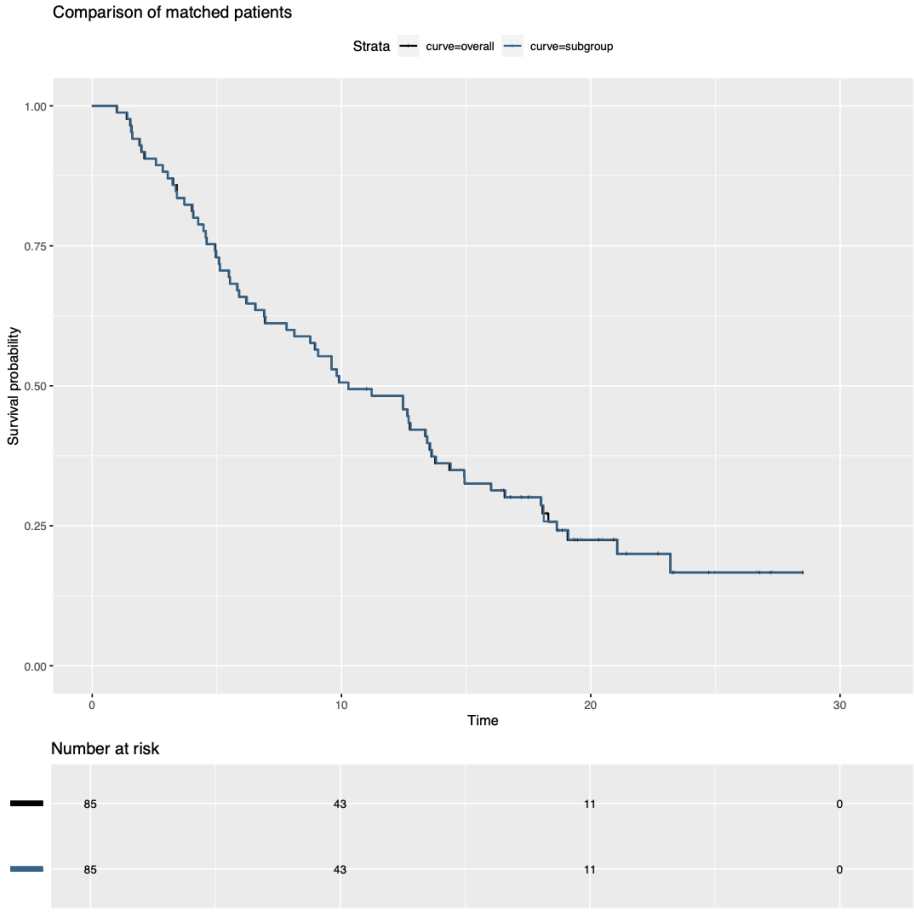
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs







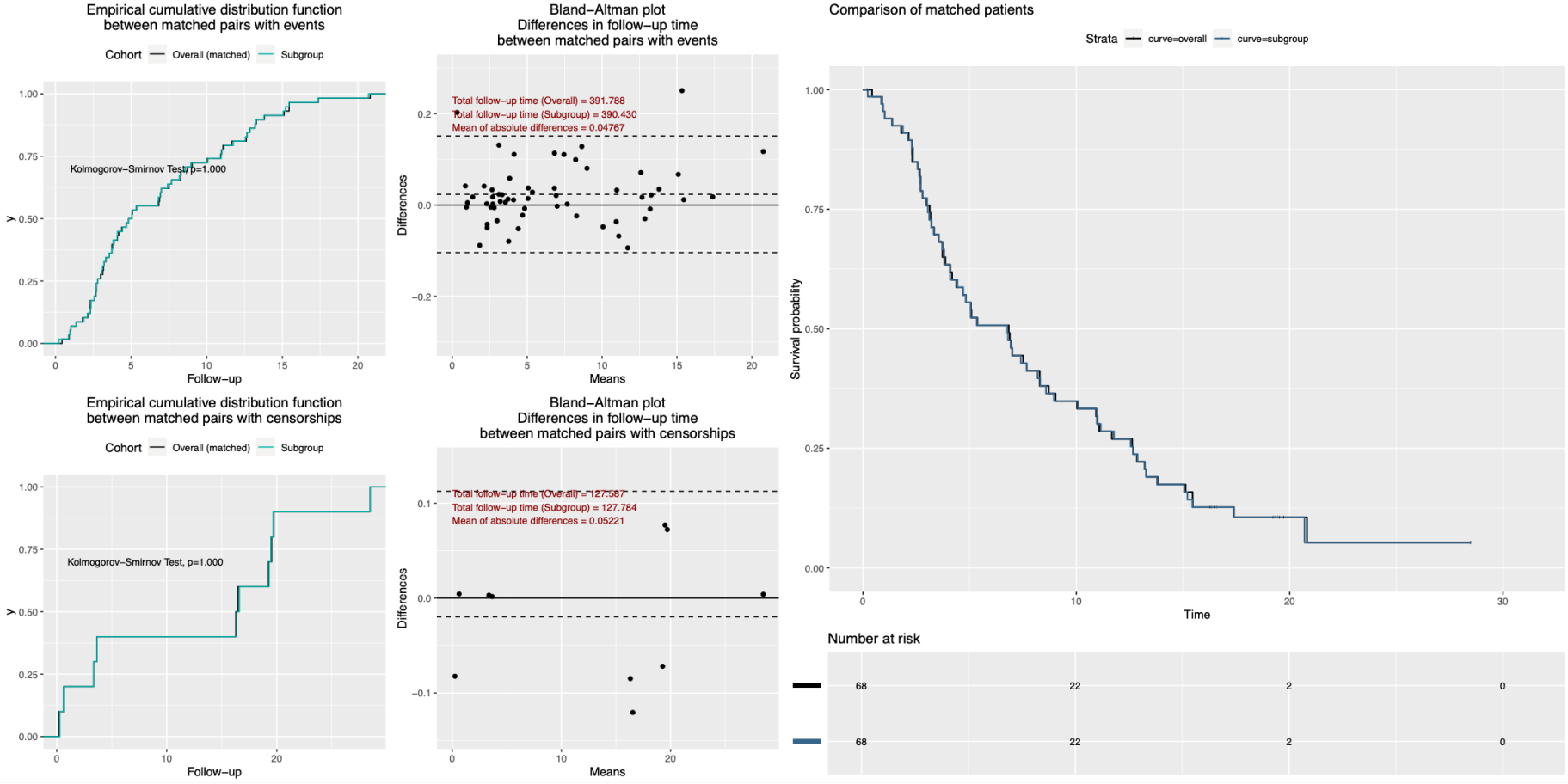




RATIONALE302 OS TAP ≥10% (Chemo)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

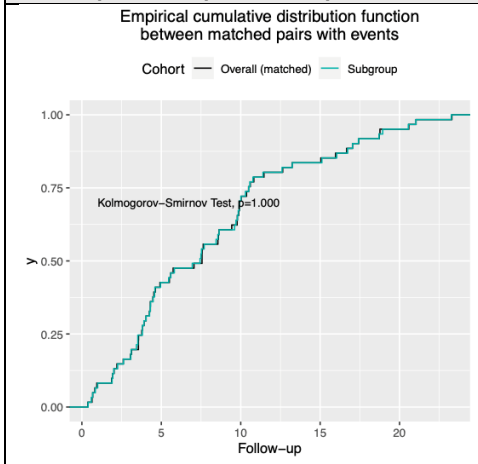
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

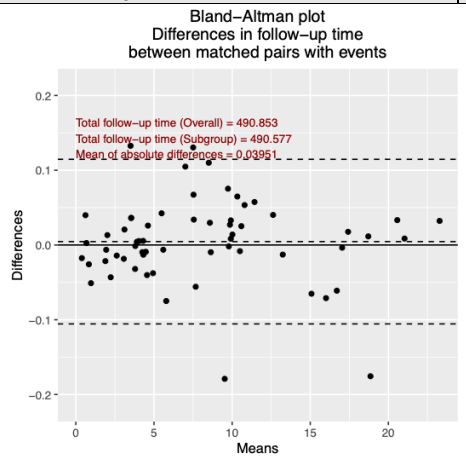


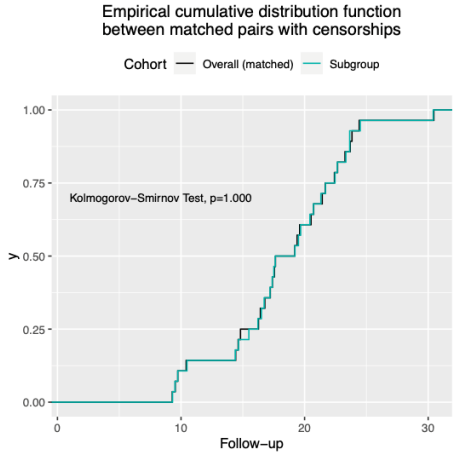
RATIONALE302 OS TAP ≥10% (Tisle)

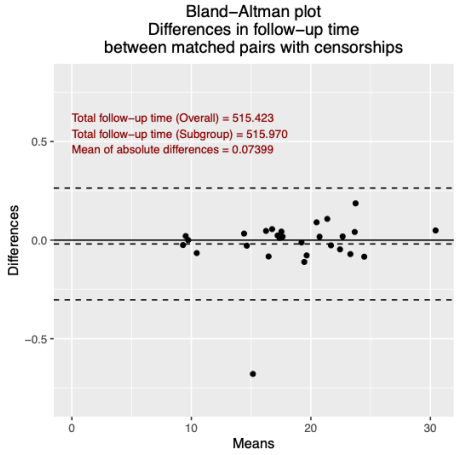
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

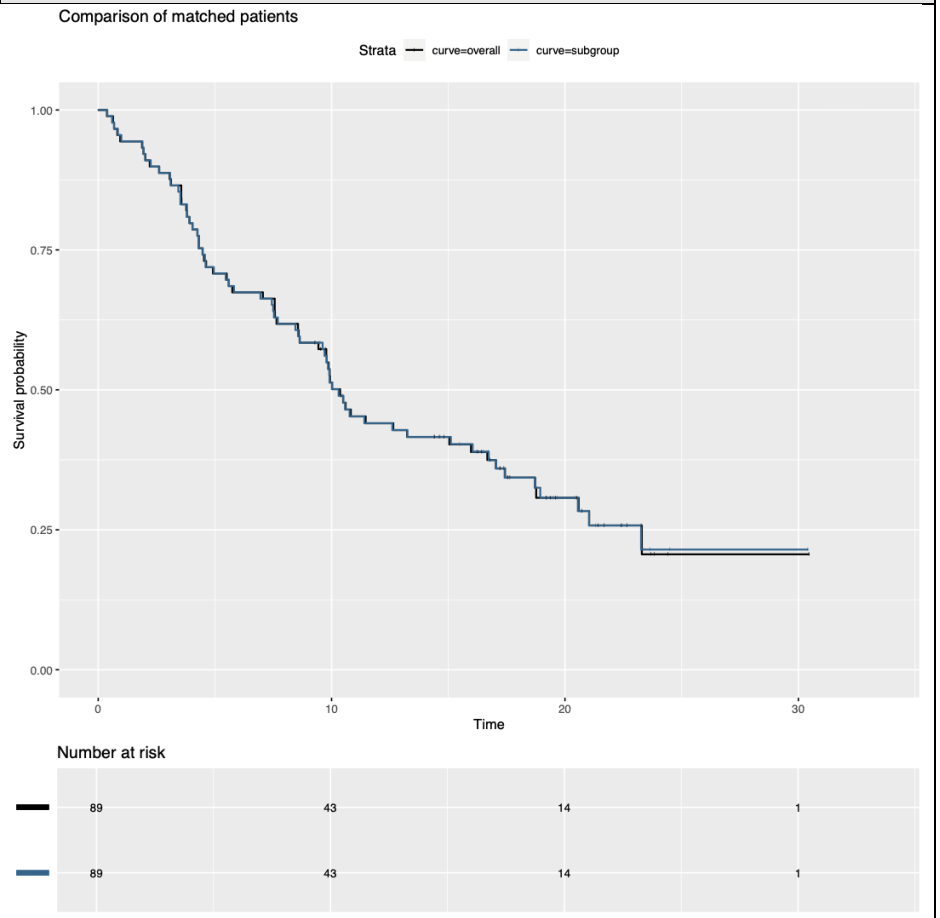
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs







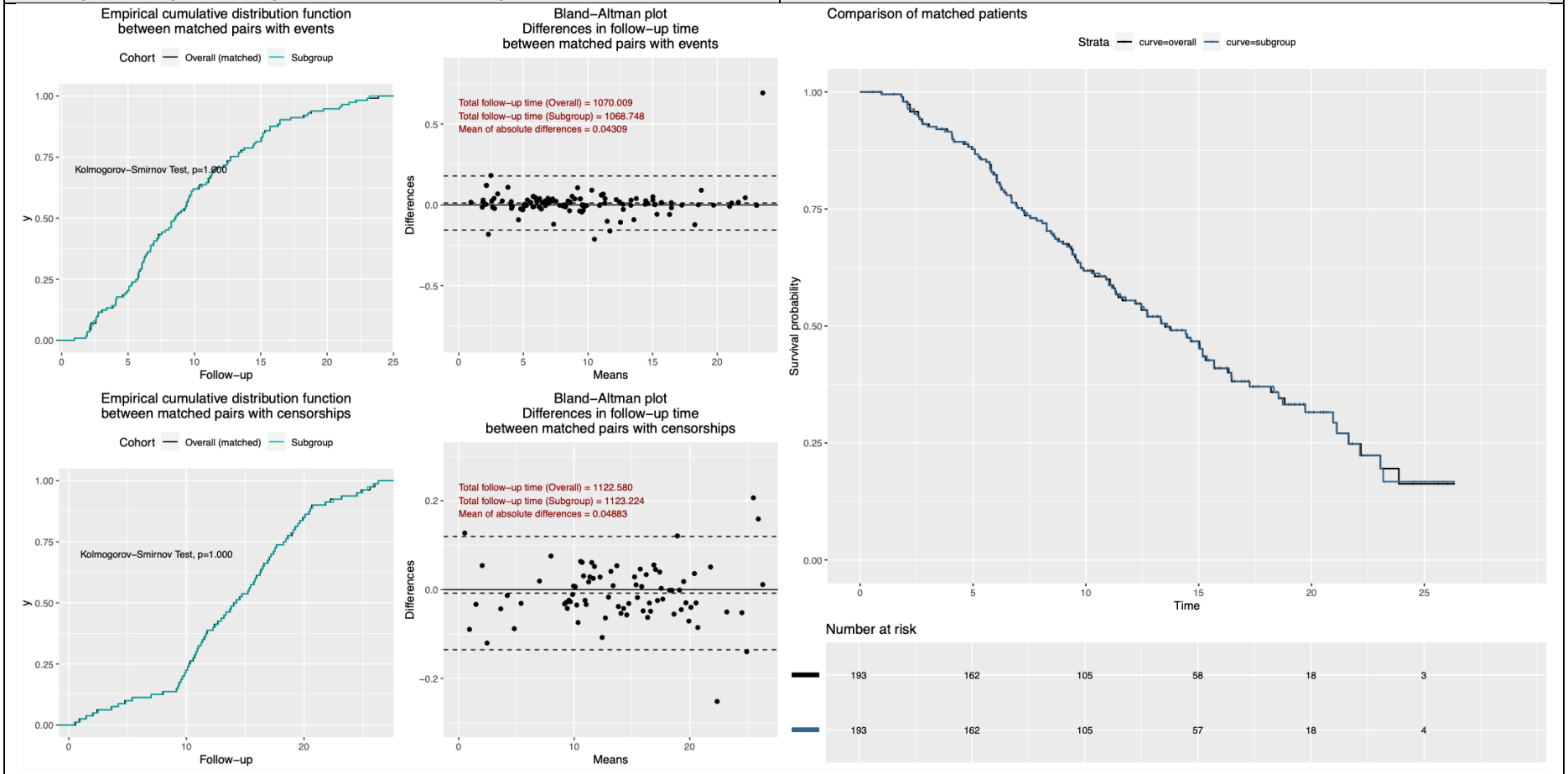




ORIENT15 OS CPS ≥10% (Chemo)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

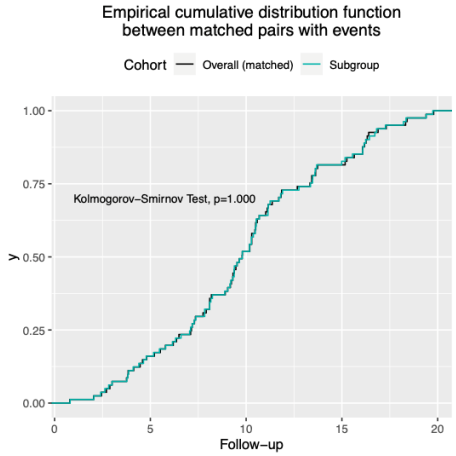
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

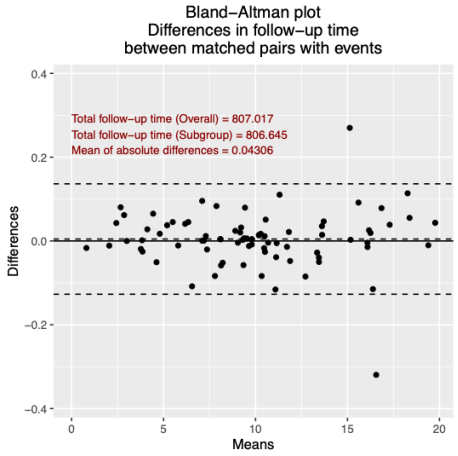


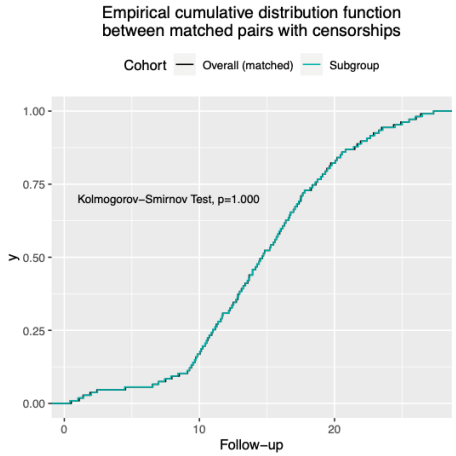
ORIENT15 OS CPS ≥10% (Sinti + Chemo)

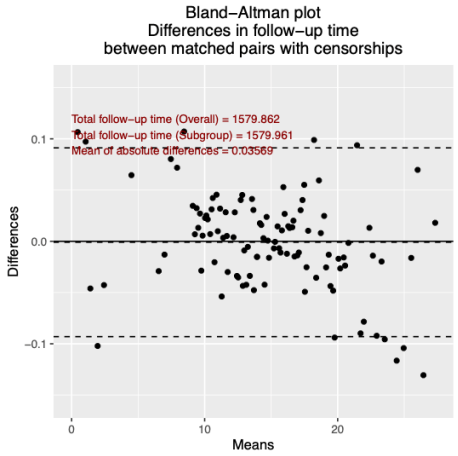
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

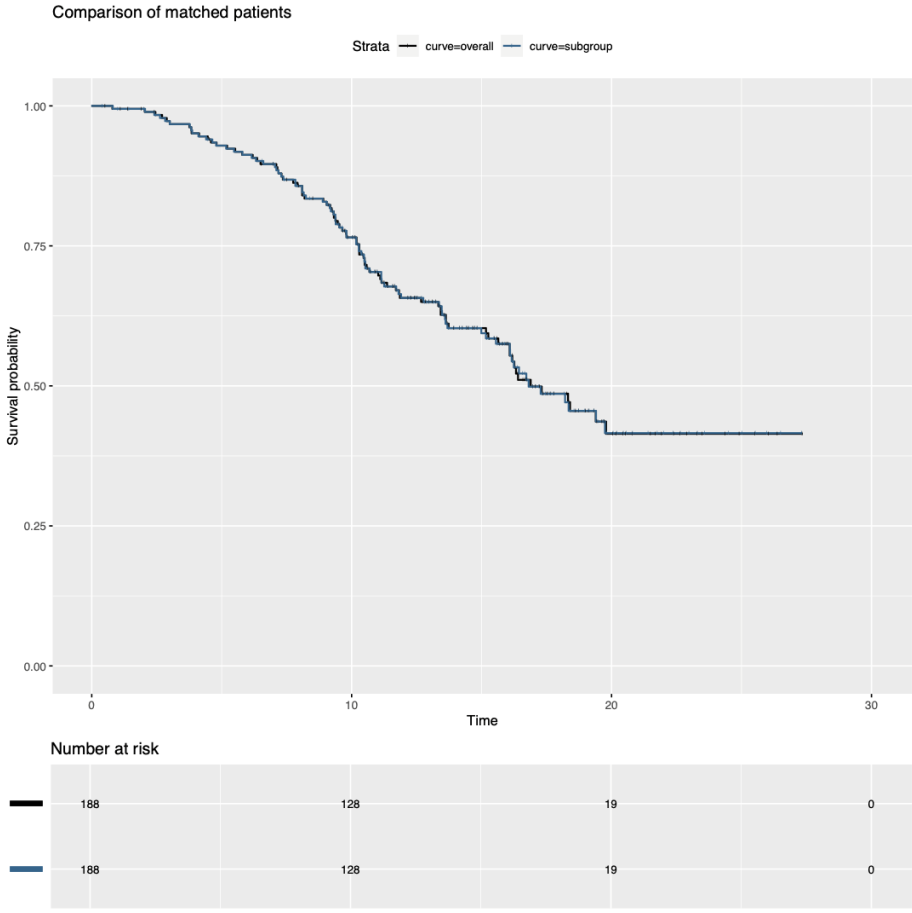
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs







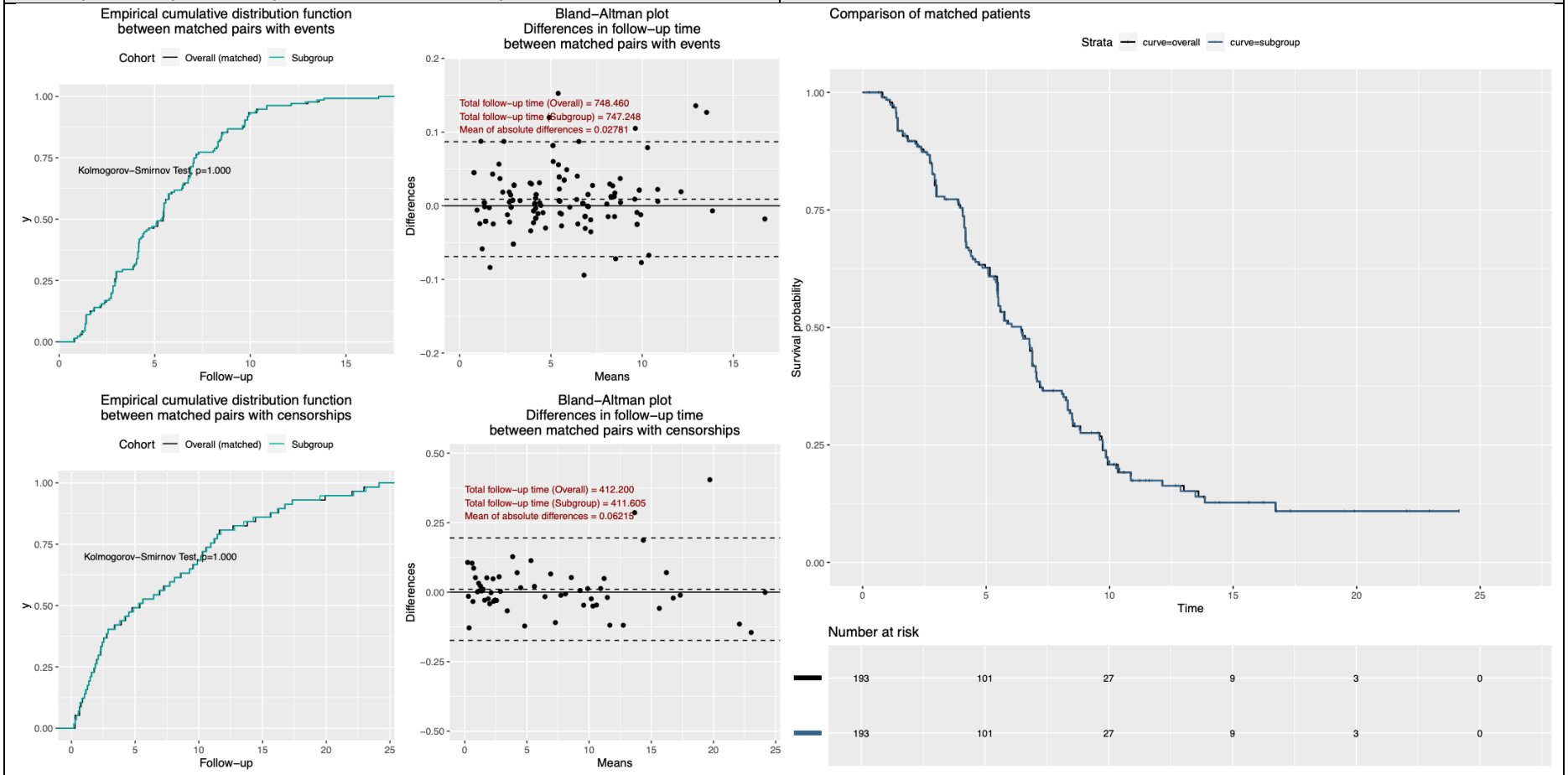




ORIENT15 PFS CPS ≥10% (Chemo)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

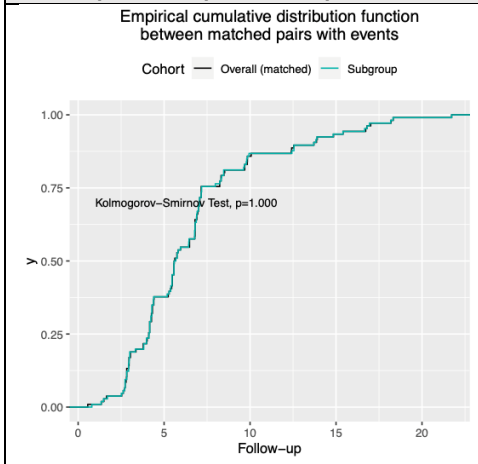
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

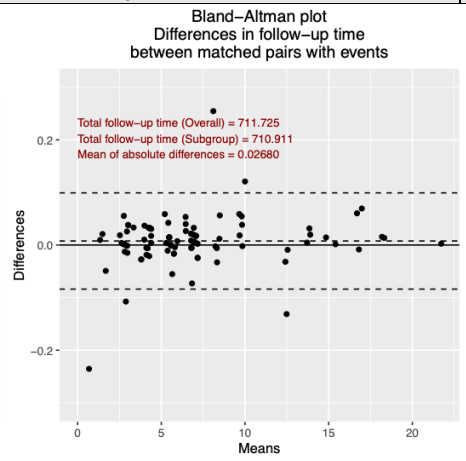


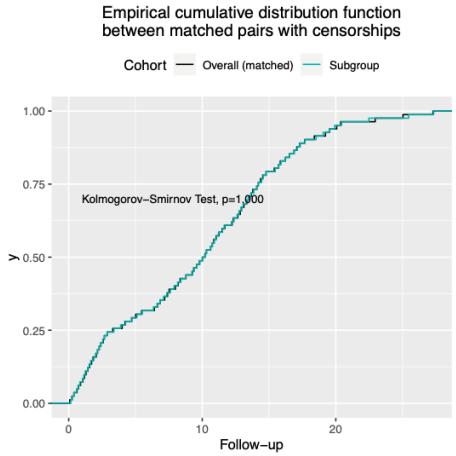
ORIENT15 PFS CPS ≥10% (Sinti + Chemo)

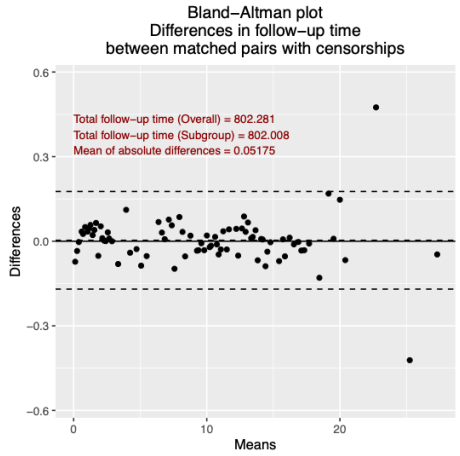
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

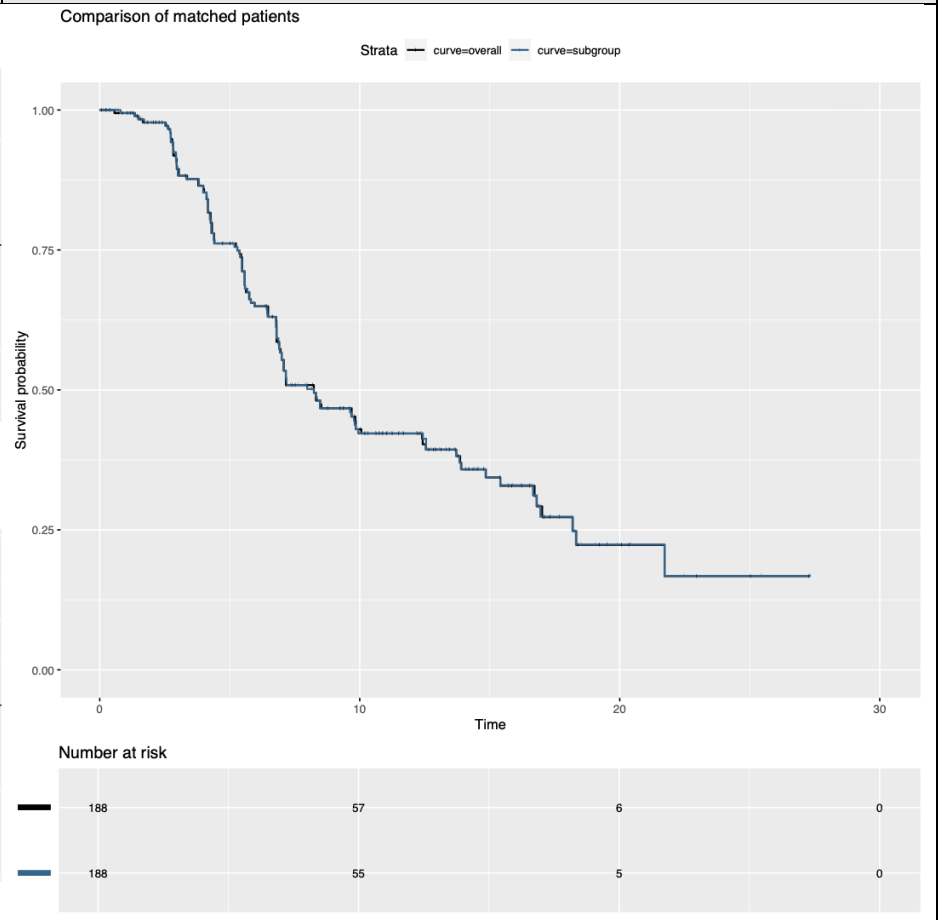
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs







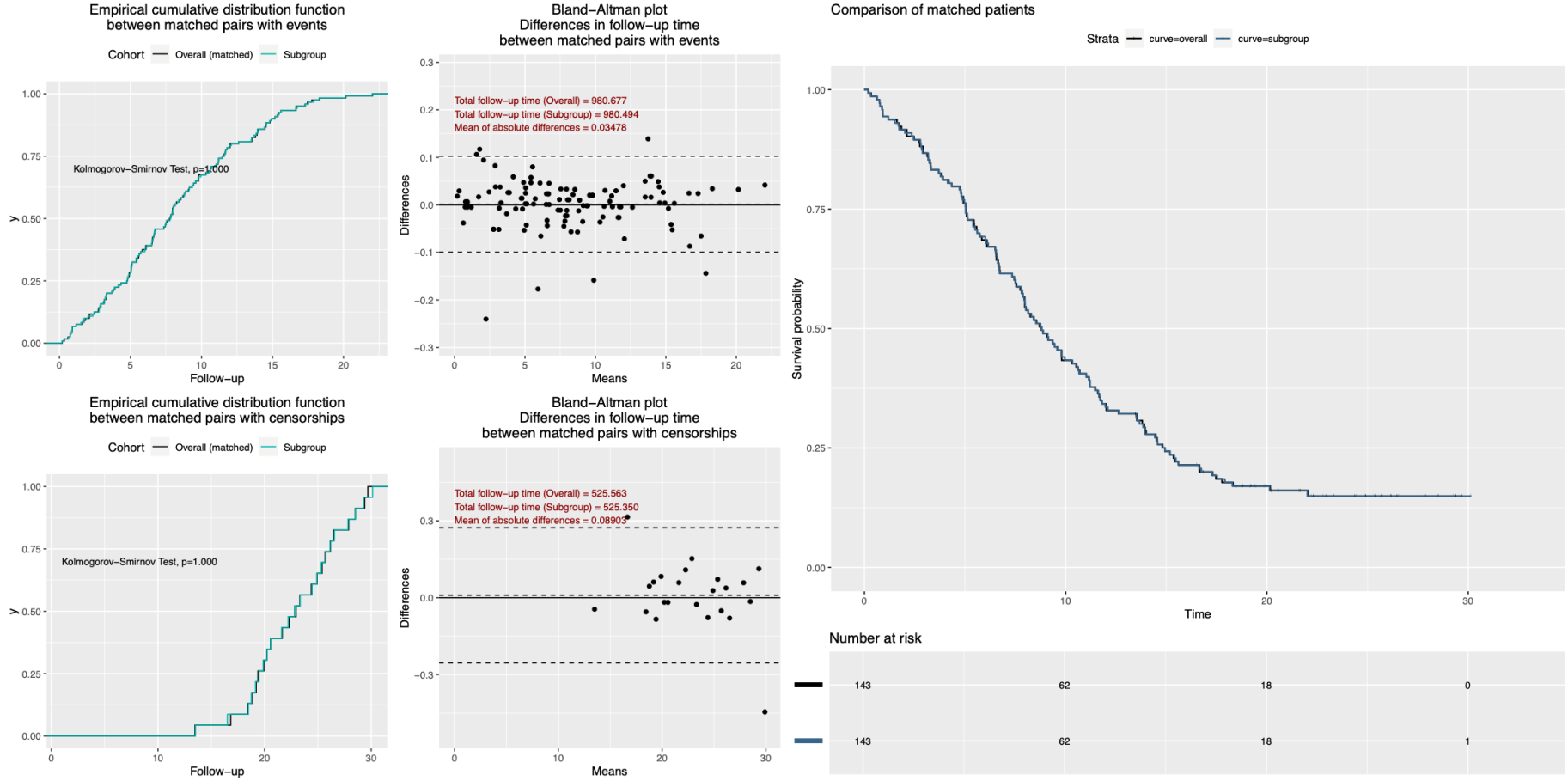




KN590 OS CPS ≥10% (Chemo)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

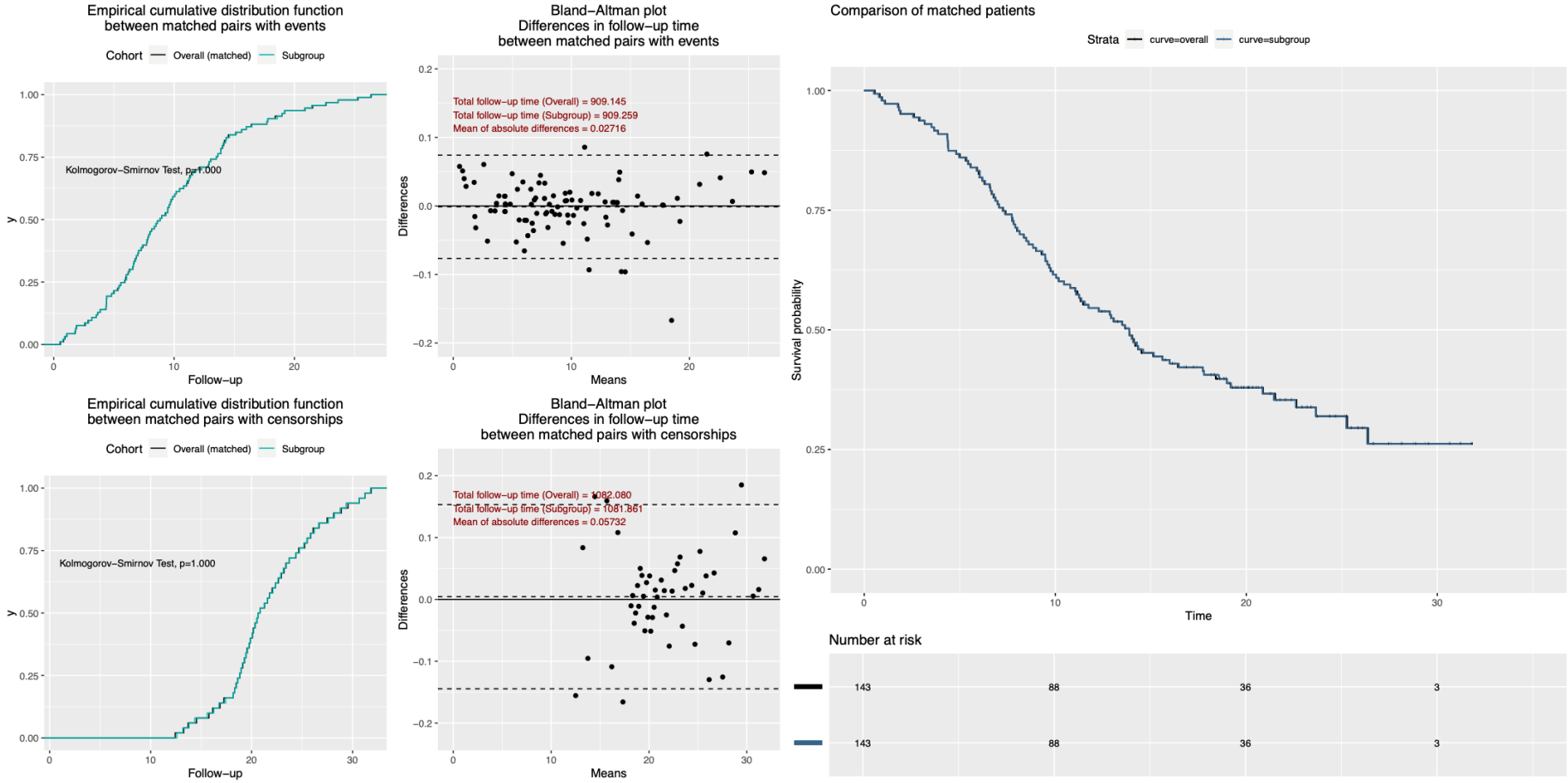
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs



KN590 OS CPS ≥10% (Pembro + Chemo)

Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

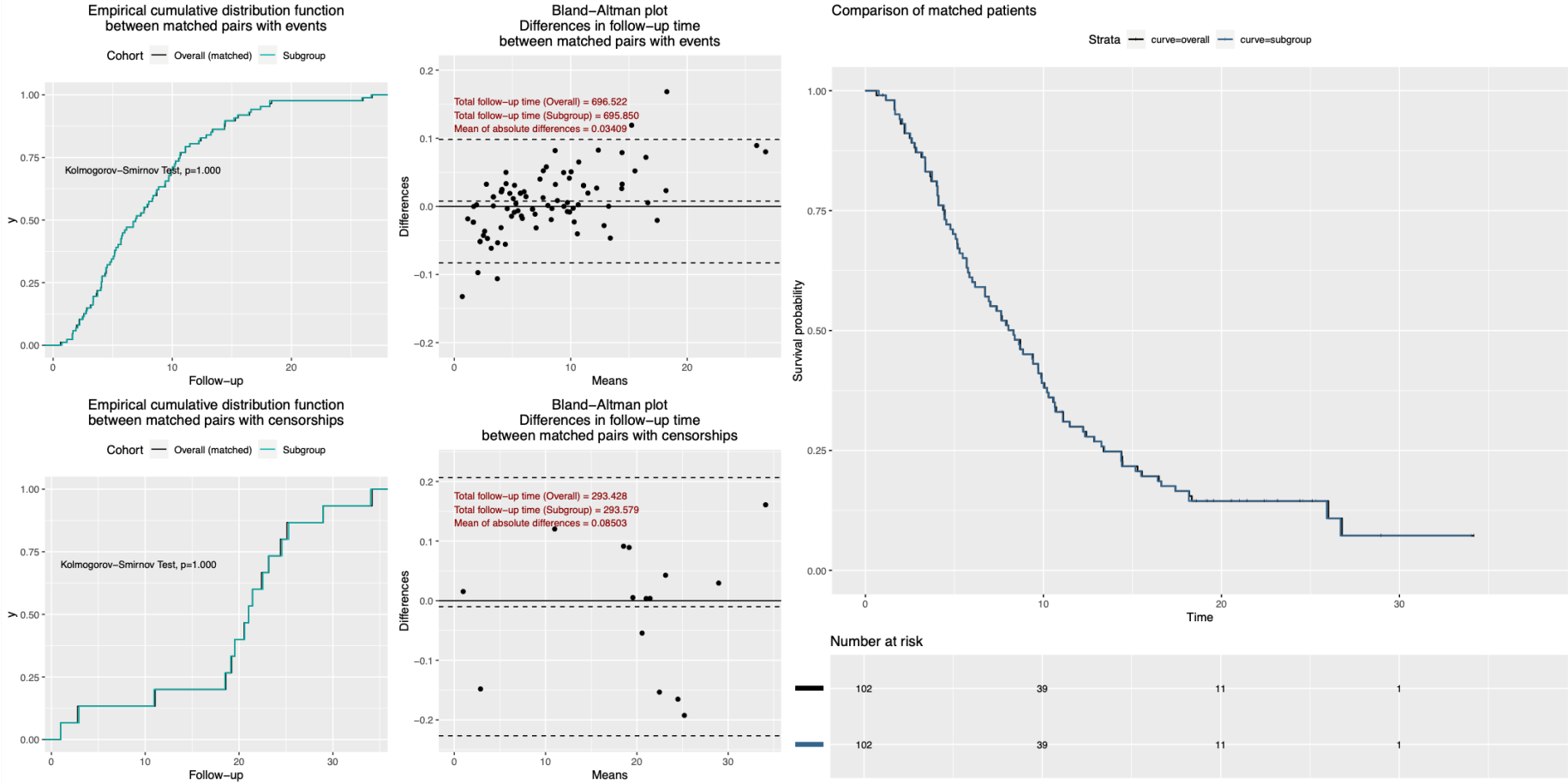
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs



ATTRACTION3 OS TPS ≥1% (Chemo)

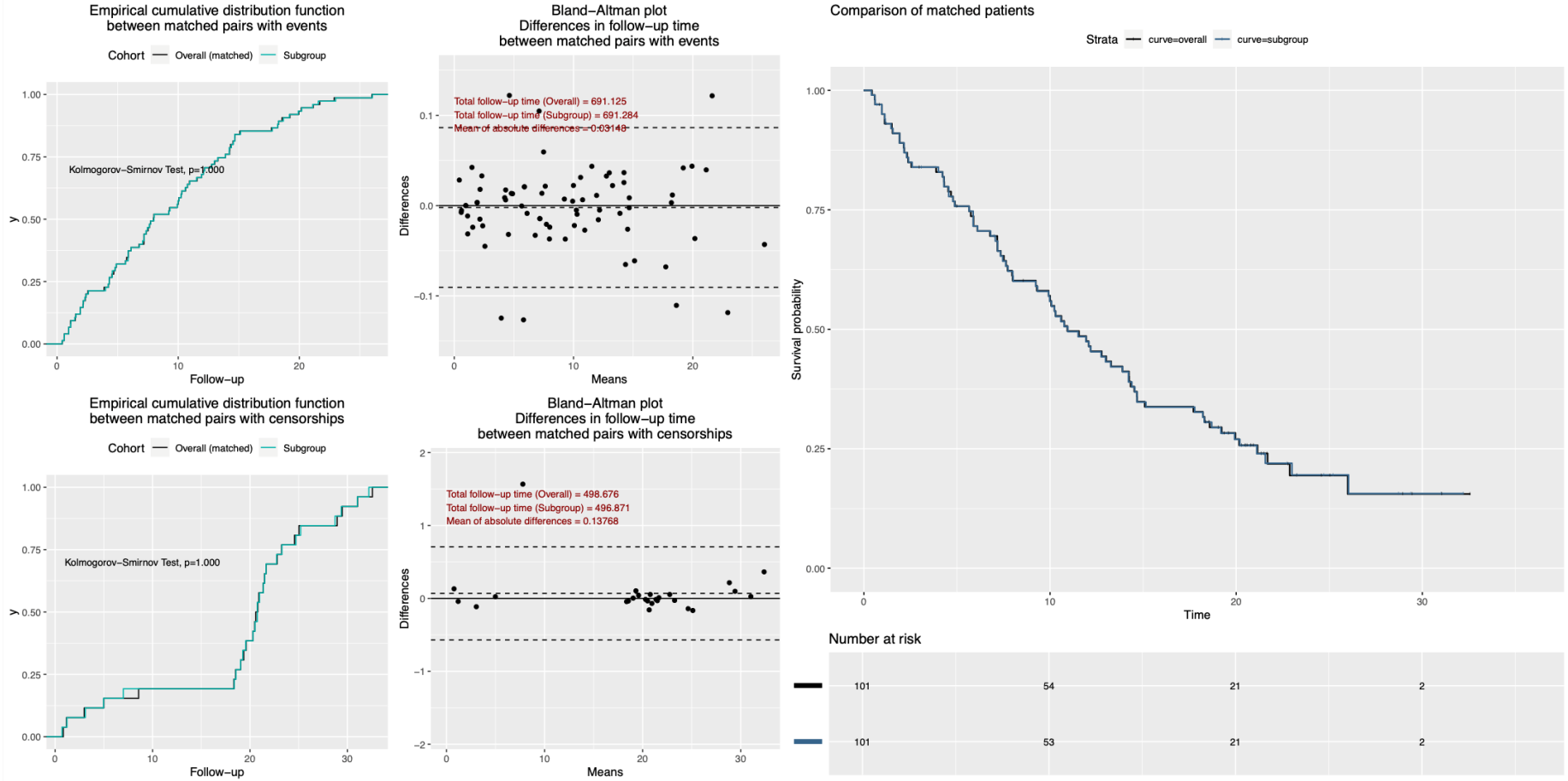
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs



ATTRACTION3 OS TPS ≥1% (Nivo)

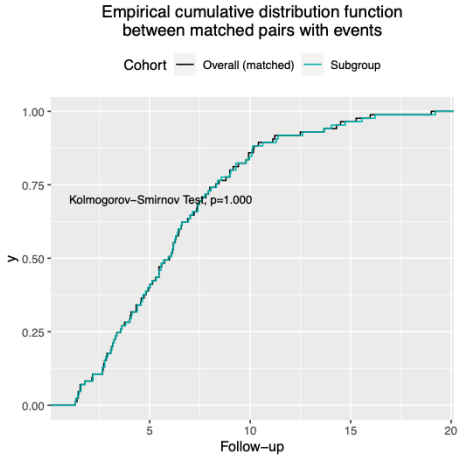
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

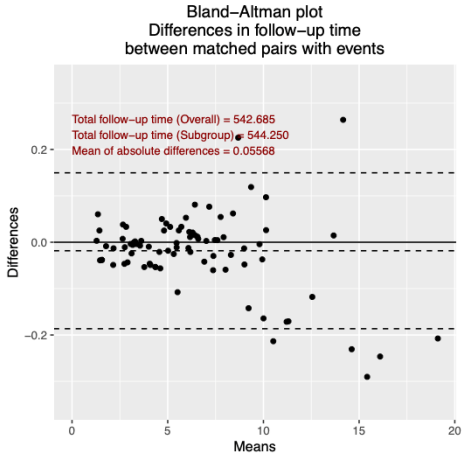


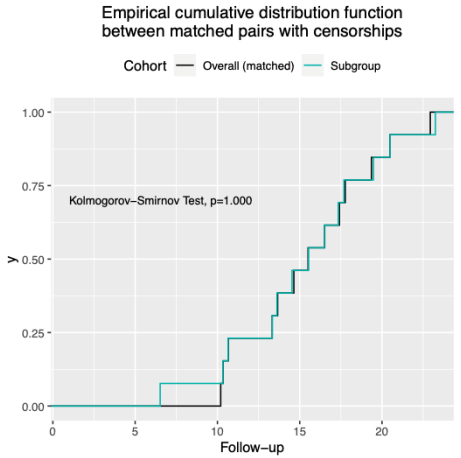
ESCORT OS TPS ≥1% (Chemo)

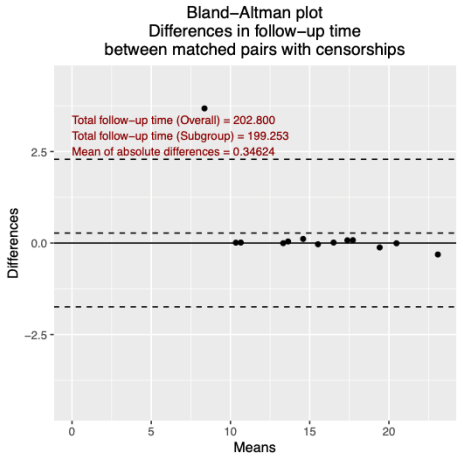
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs

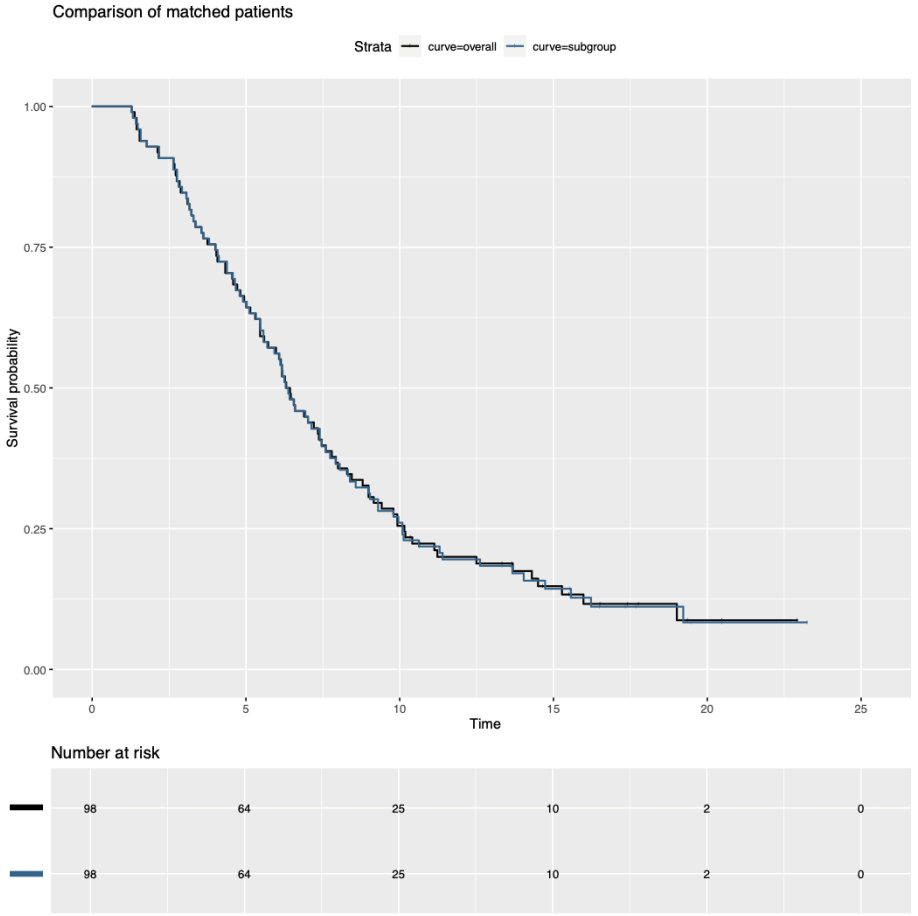
Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs





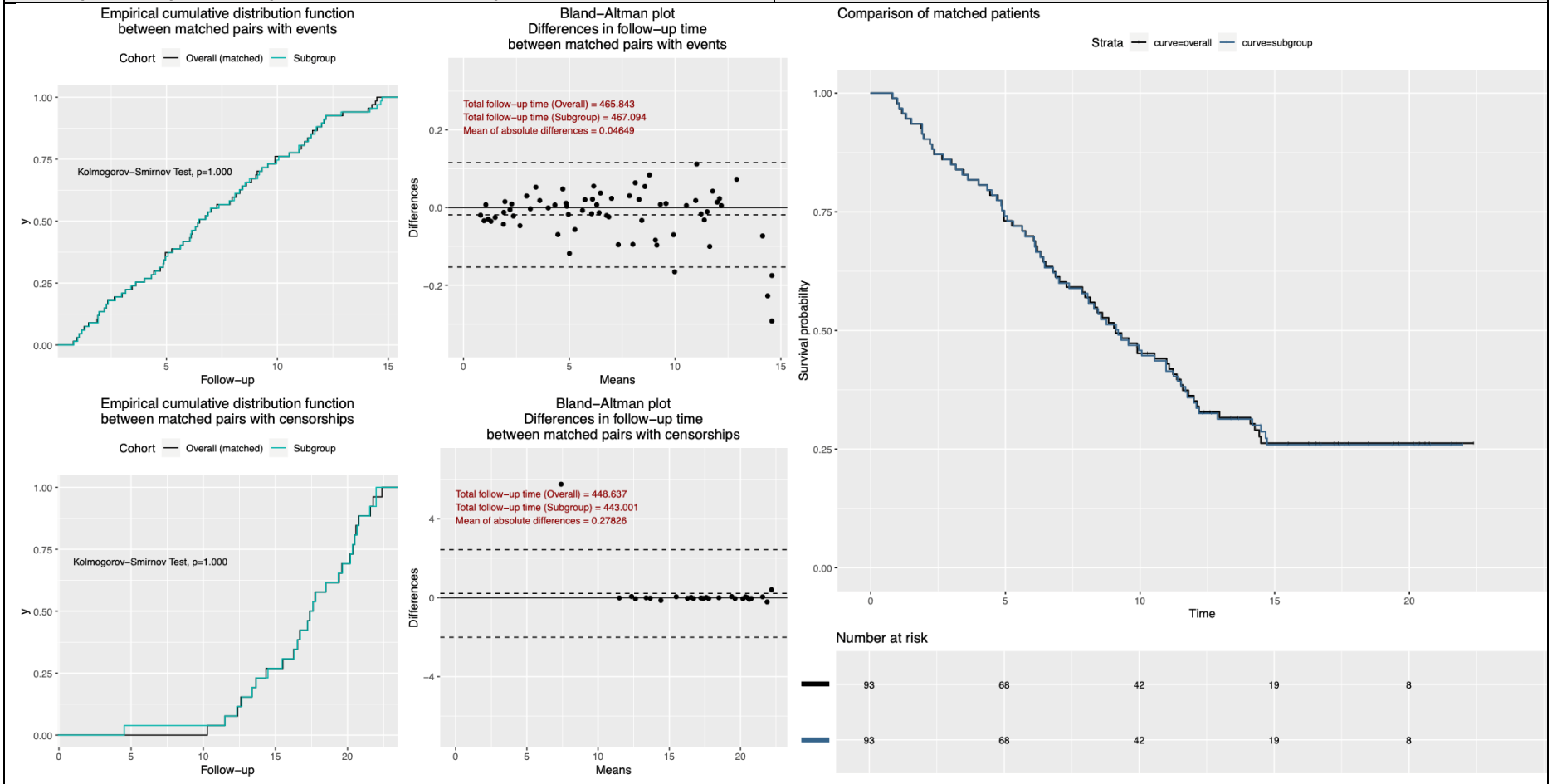






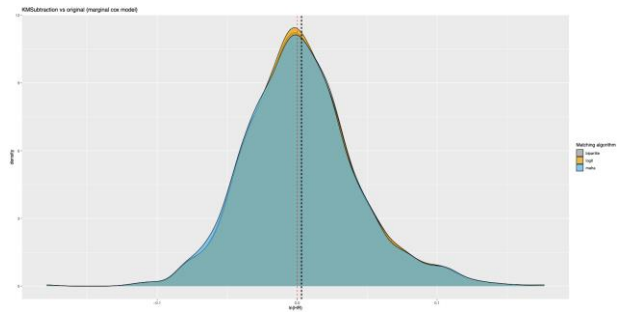
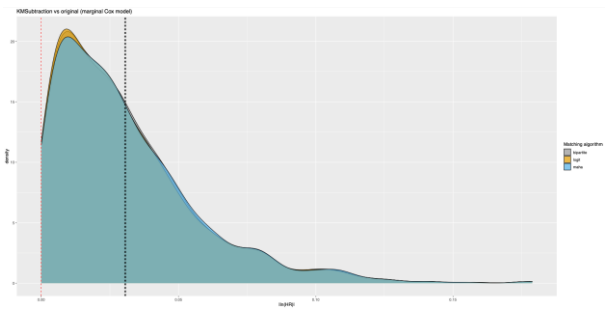
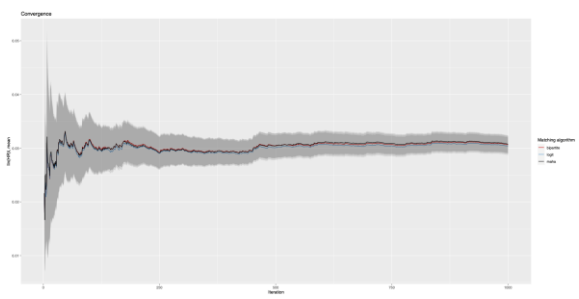
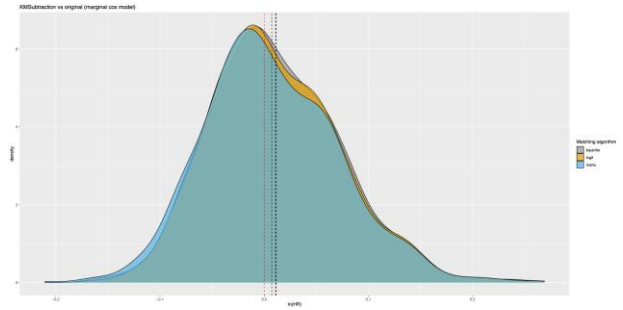
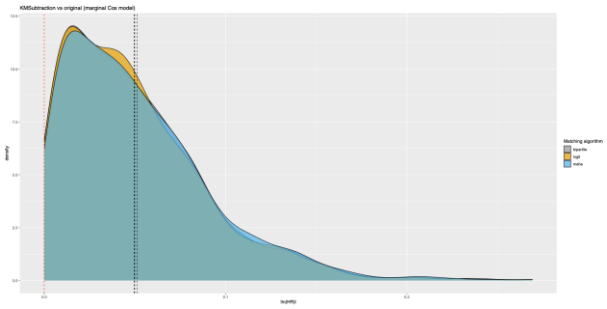
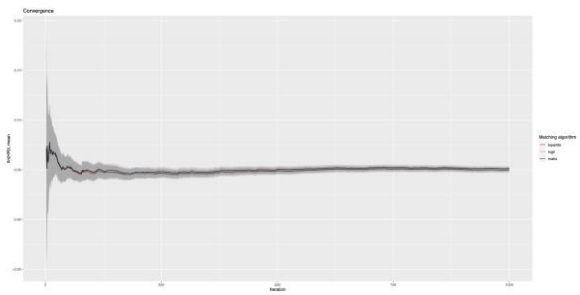
ESCORT OS TPS ≥1% (Camre)

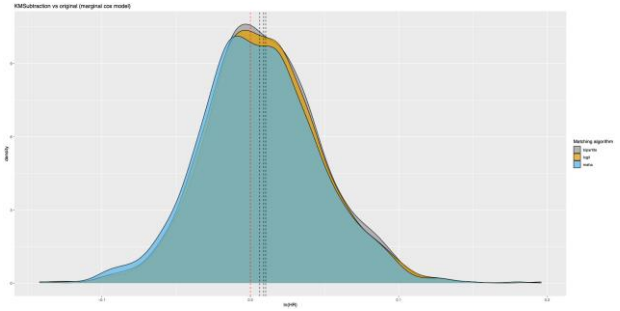
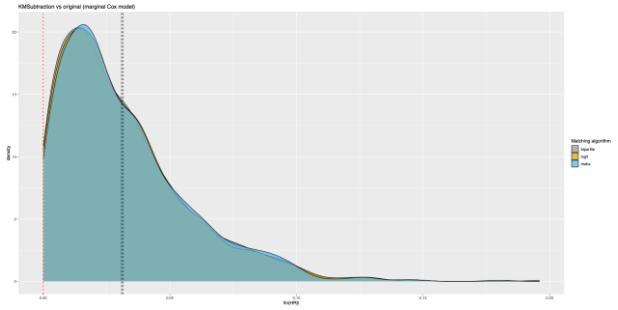
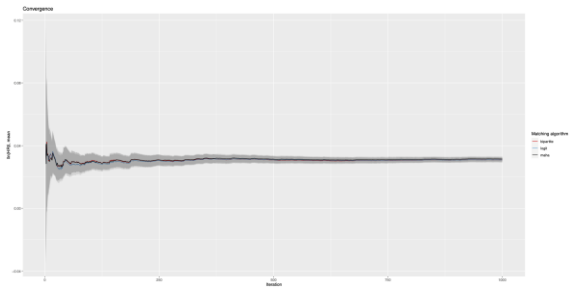
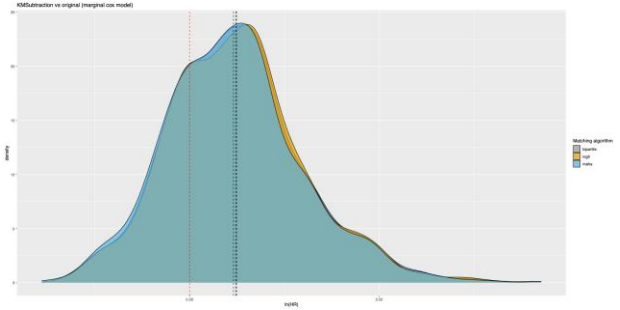
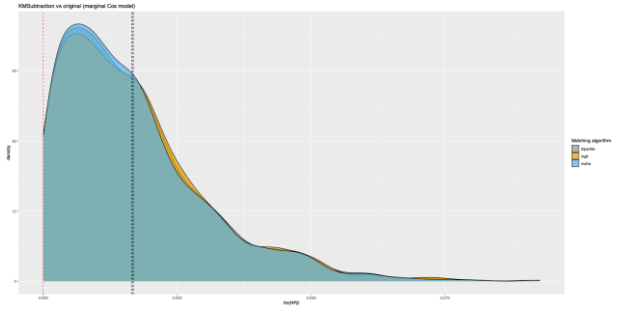
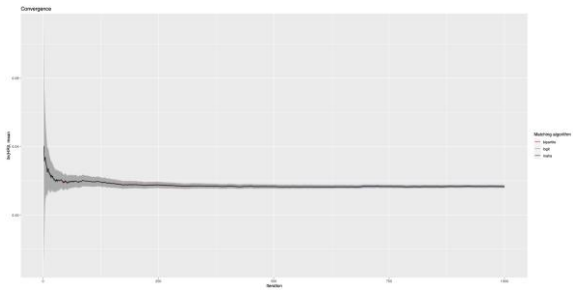
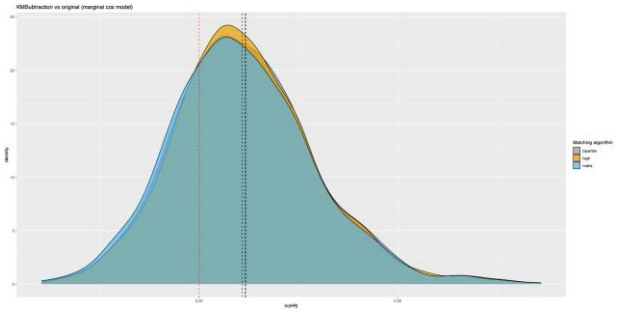
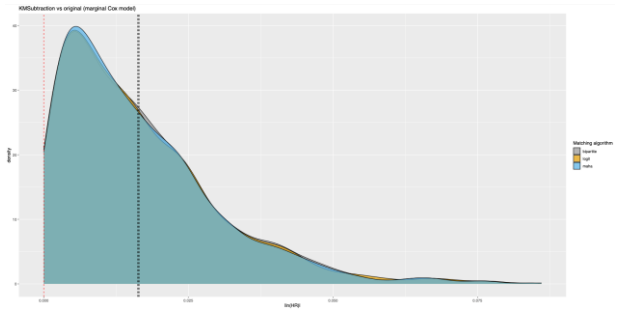
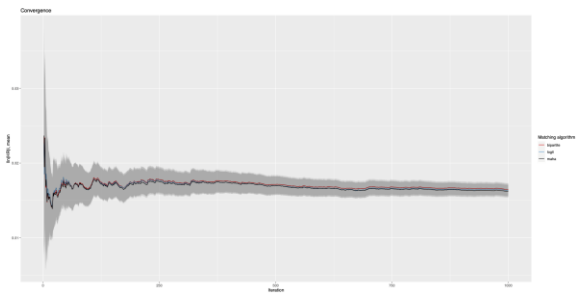
Empirical cumulative distribution between follow-up time of matched pairs and Bland-Altman plots to explore discrepancies between matched pairs	Kaplan Meier Curves and Cox-proportional hazard's model comparing matched pairs

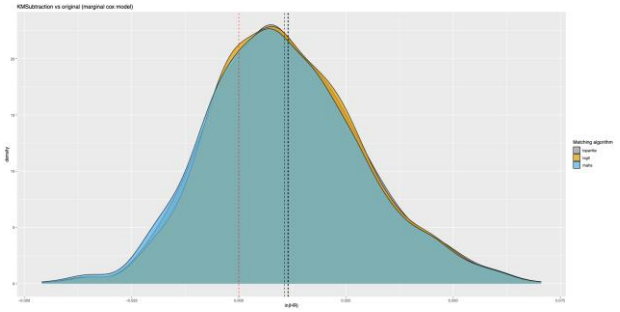
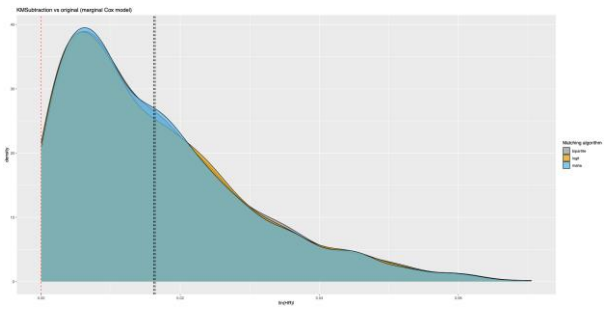
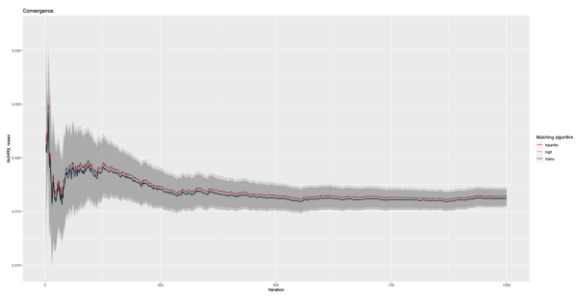
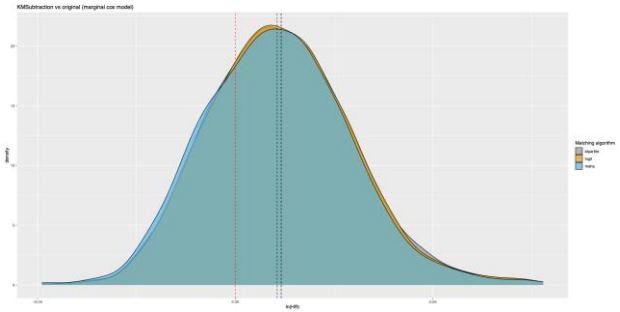
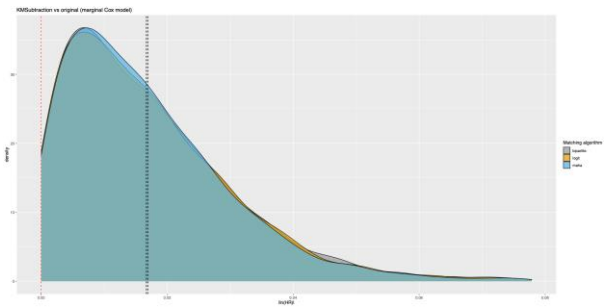
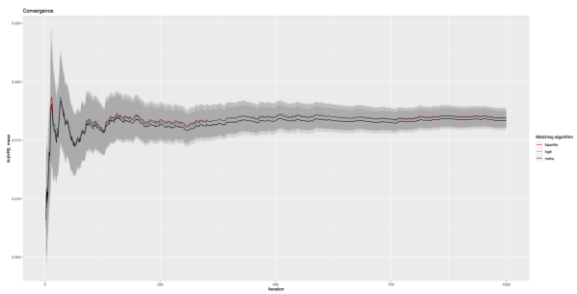
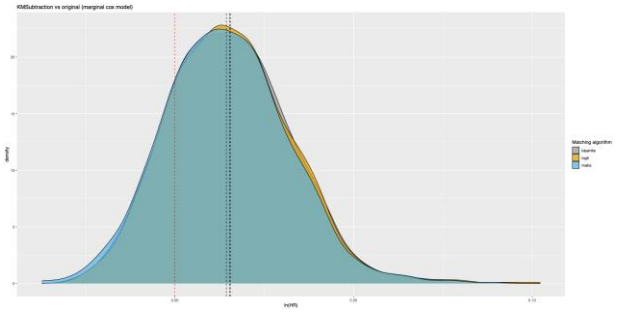
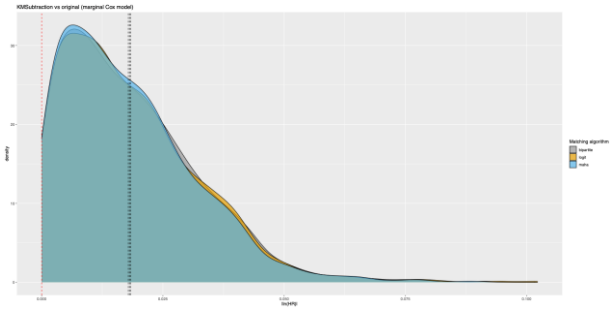
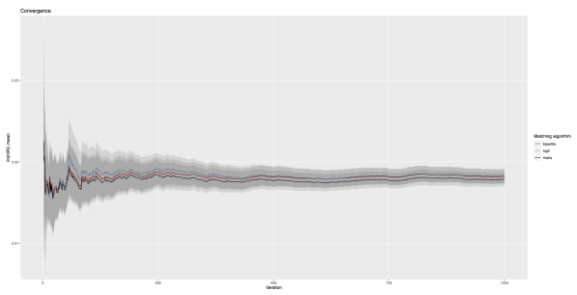


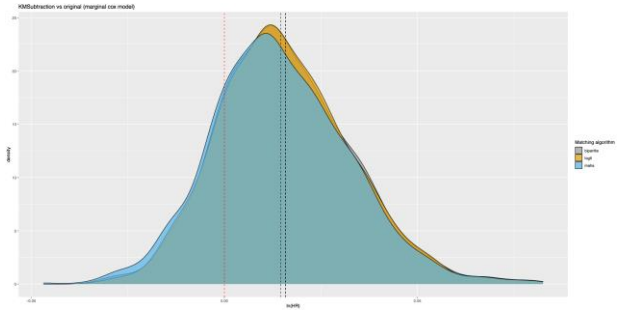
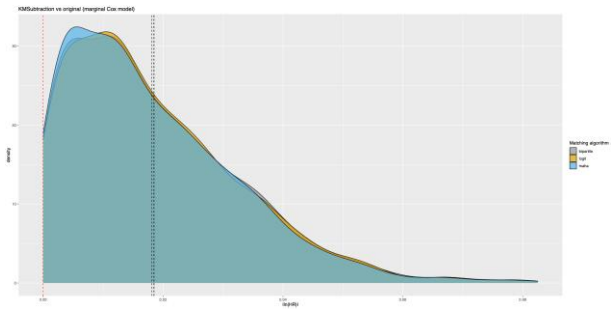
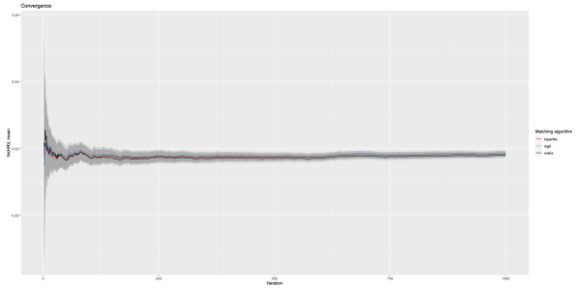
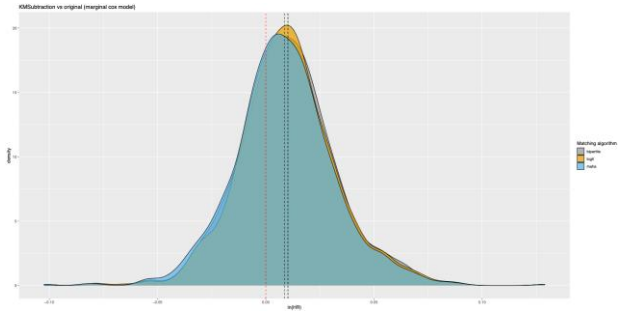
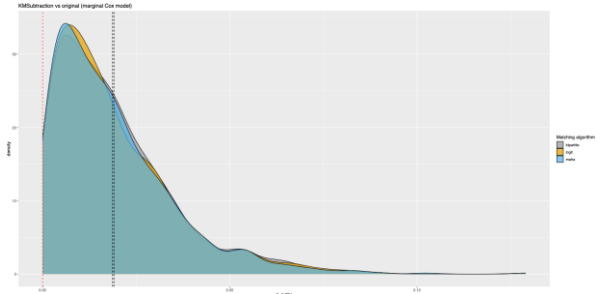
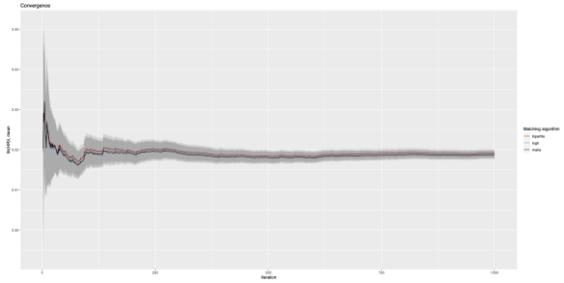
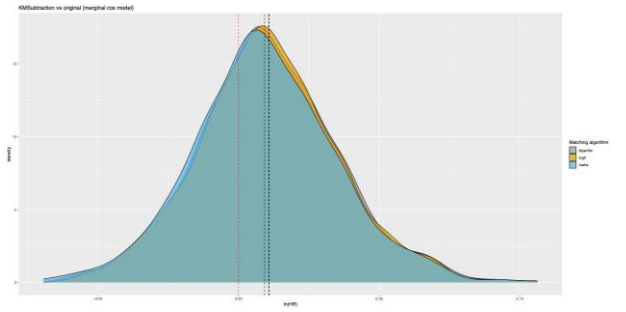
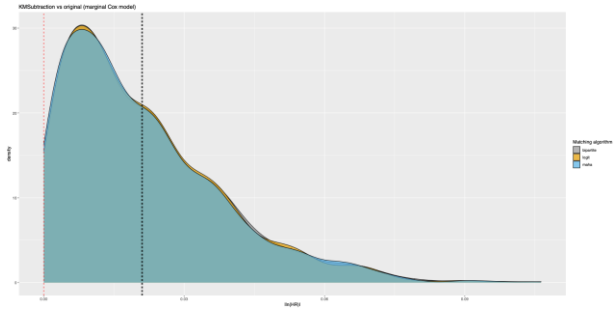
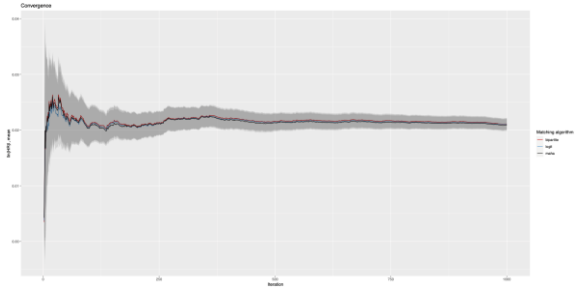
Abbreviations: Nivo, nivolumab; Ipi, ipilimumab; Camre, camrelizumab; Pembro, pembrolizumab; Sinti, sintilimab; Tisle, Tislelizumab; Chemo, chemotherapy; CPS, combined positive score; TPS, tumor proportion score; TAP, tumor area positivity; CM648, CheckMate 648; KN590, KEYNOTE-590; KN181, KEYNOTE-181.

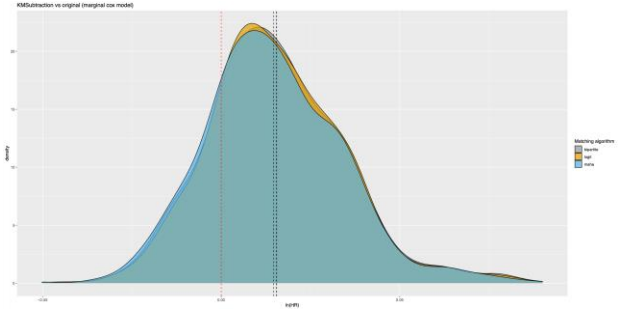
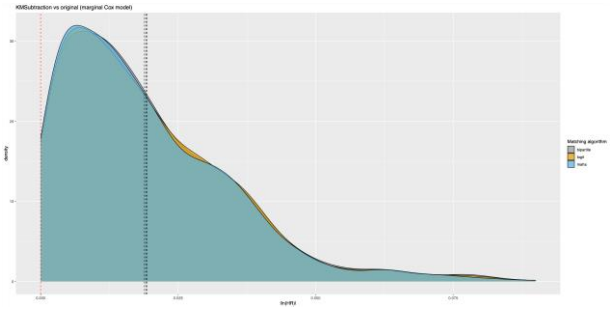
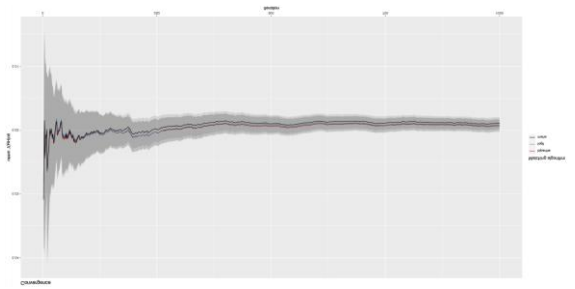
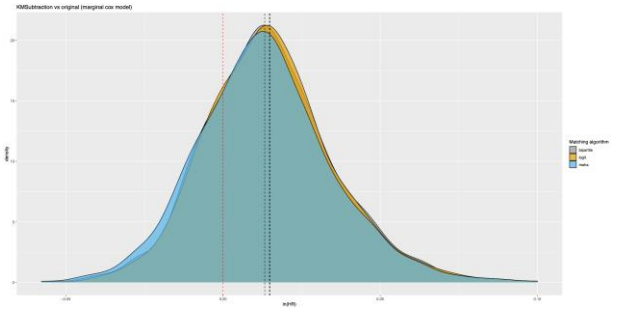
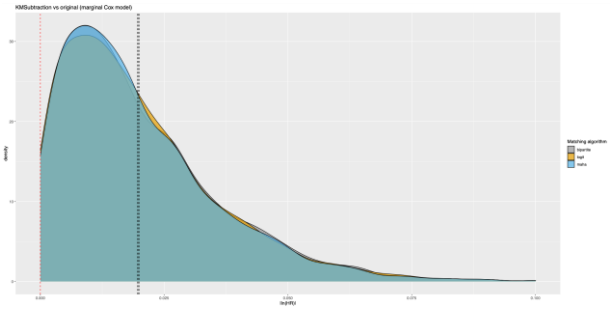
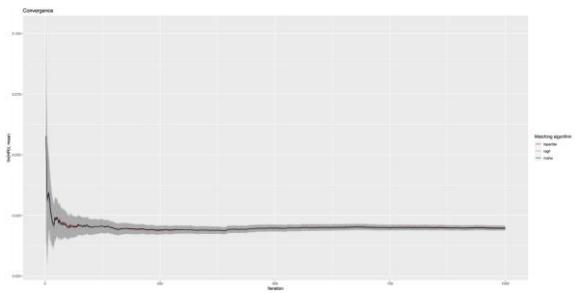
eFigure 6. Convergence Plots and Histograms of Simulations

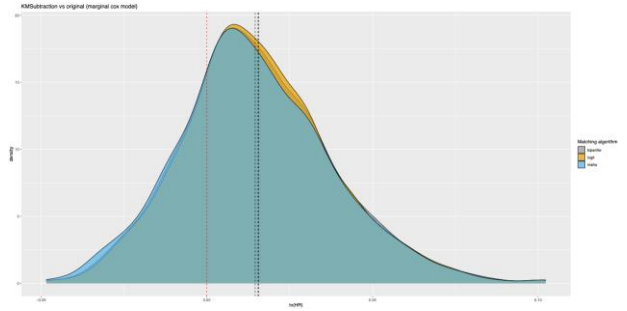
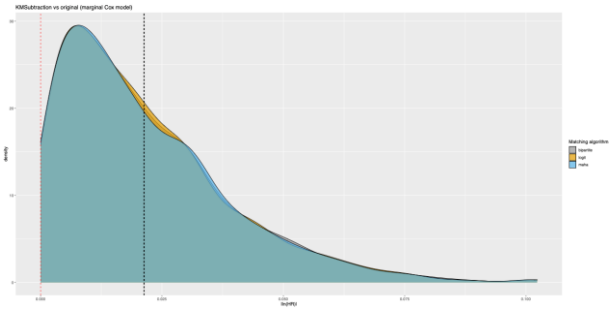
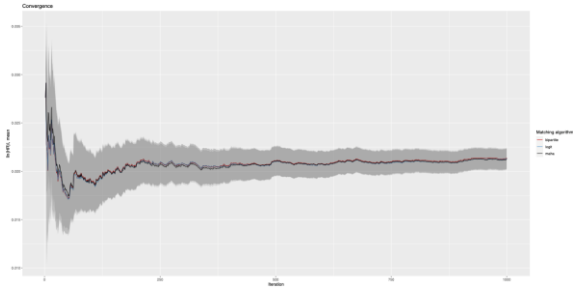
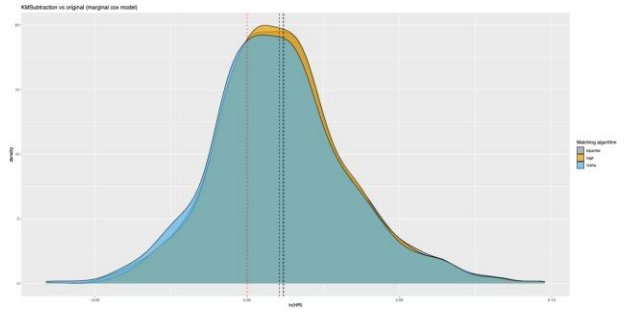
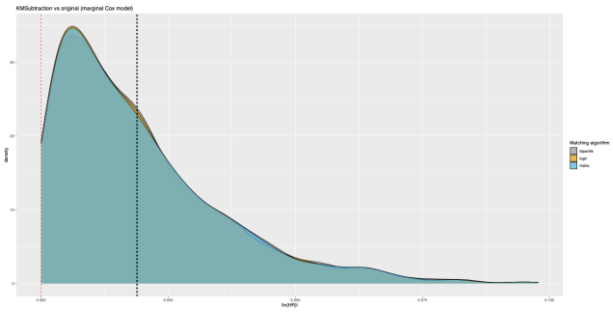
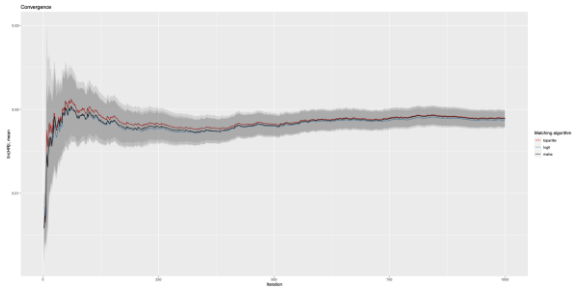
Histogram of ln(HR) CM648, DOR, Chemo, TPS≥1%	Histogram of |ln(HR)| CM648, DOR, Chemo, TPS≥1%	Convergence plot CM648, DOR, Chemo, TPS≥1%
		
Histogram of ln(HR) CM648, DOR, Nivo+Ipi, TPS≥1%	Histogram of |ln(HR)| CM648, DOR, Nivo+Ipi, TPS≥1%	Convergence plot CM648, DOR, Nivo+Ipi, TPS≥1%
		

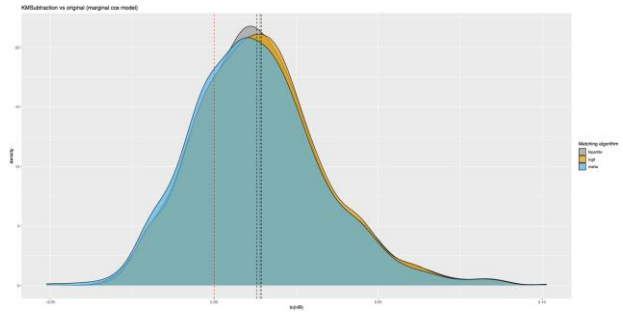
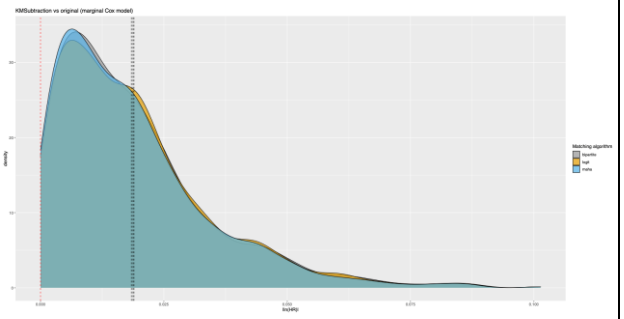
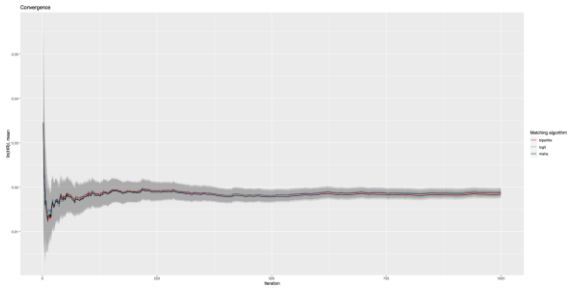
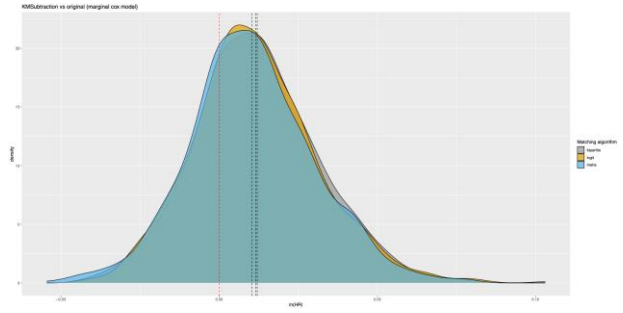
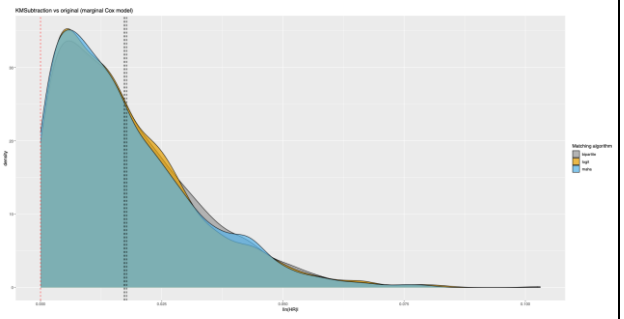
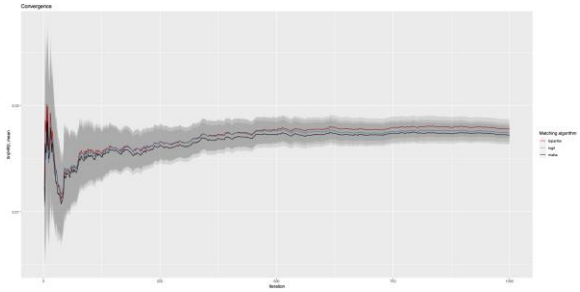
Histogram of ln(HR) CM648, DOR, Nivo+Chemo, TPS≥1%	Histogram of |ln(HR)| CM648, DOR, Nivo+Chemo, TPS≥1%	Convergence plot CM648, DOR, Nivo+Chemo, TPS≥1%
		
Histogram of ln(HR) CM648, OS, Chemo, TPS≥1%	Histogram of |ln(HR)| CM648, OS, Chemo, TPS≥1%	Convergence plot CM648, OS, Chemo, TPS≥1%
		
Histogram of ln(HR) CM648, OS, Nivo+Ipi, TPS≥1%	Histogram of |ln(HR)| CM648, OS, Nivo+Ipi, TPS≥1%	Convergence plot CM648, OS, Nivo+Ipi, TPS≥1%
		

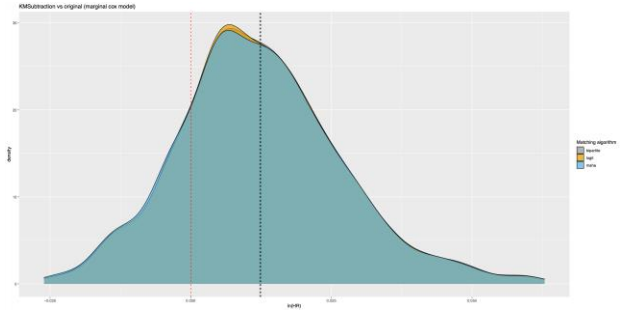
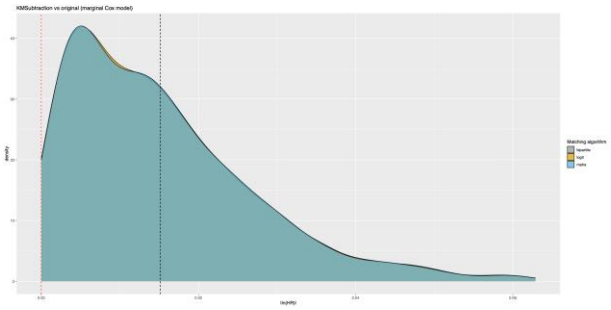
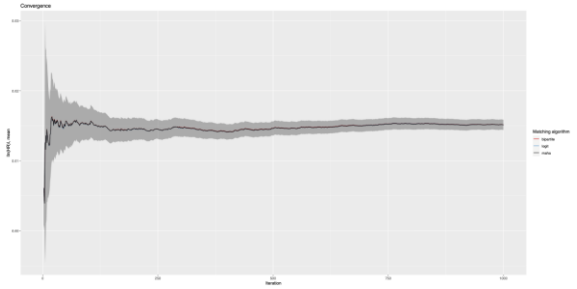
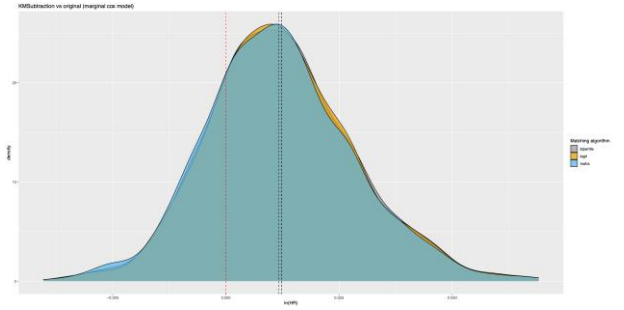
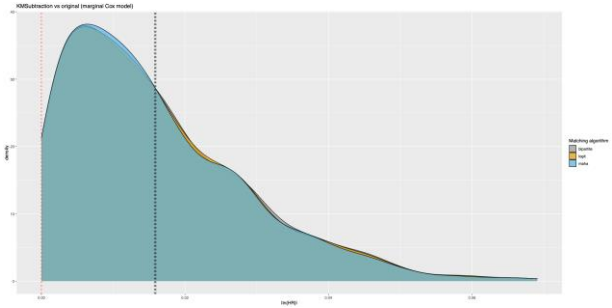
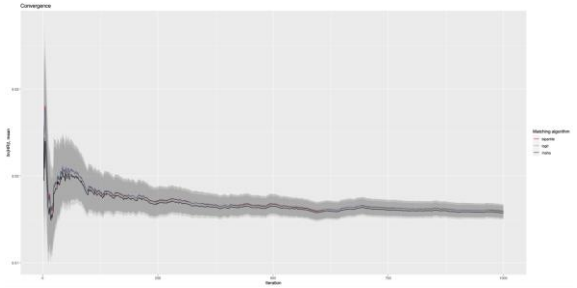
Histogram of ln(HR) CM648, OS, Nivo+Chemo, TPS≥1%	Histogram of |ln(HR)| CM648, OS, Nivo+Chemo, TPS≥1%	Convergence plot CM648, OS, Nivo+Chemo, TPS≥1%
		
Histogram of ln(HR) CM648, PFS, Chemo, TPS≥1%	Histogram of |ln(HR)| CM648, PFS, Chemo, TPS≥1%	Convergence plot CM648, PFS, Chemo, TPS≥1%
		
Histogram of ln(HR) CM648, PFS, Nivo+Ipi, TPS≥1%	Histogram of |ln(HR)| CM648, PFS, Nivo+Ipi, TPS≥1%	Convergence plot CM648, PFS, Nivo+Ipi, TPS≥1%
		

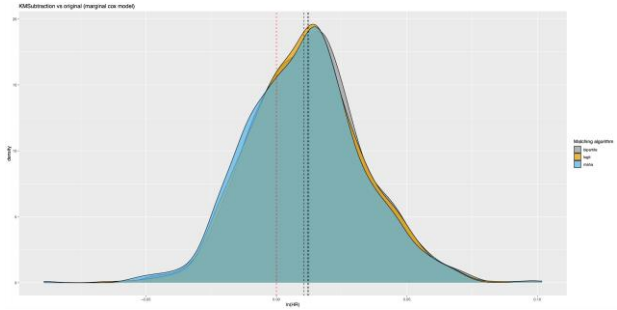
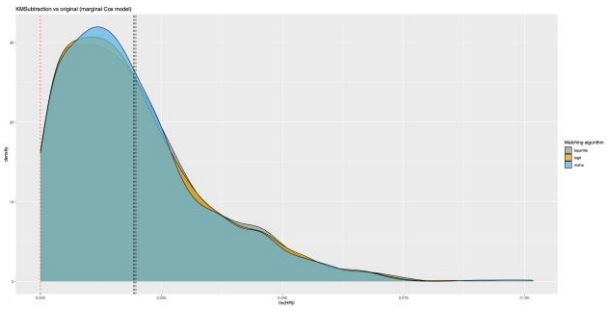
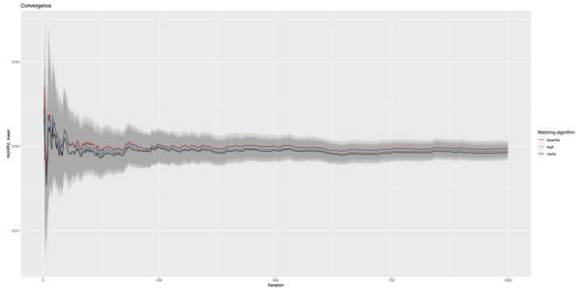
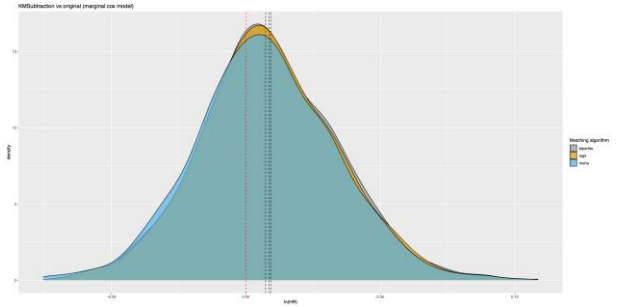
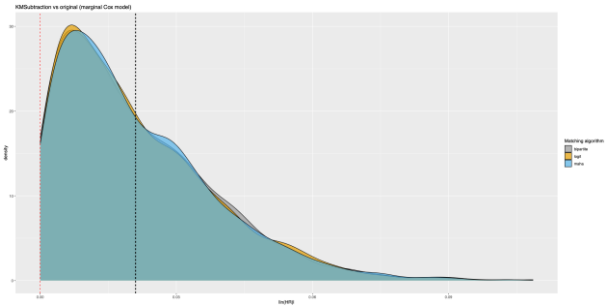
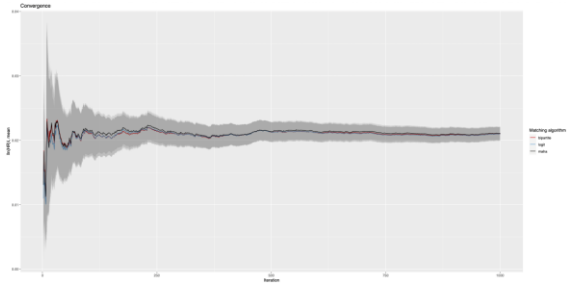
Histogram of ln(HR) CM648, PFS, Nivo+Chemo, TPS≥1%	Histogram of |ln(HR)| CM648, PFS, Nivo+Chemo, TPS≥1%	Convergence plot CM648, PFS, Nivo+Chemo, TPS≥1%
		
Histogram of ln(HR) Escort1st, OS, Chemo, TPS≥1%	Histogram of |ln(HR)| Escort1st, OS, Chemo, TPS≥1%	Convergence plot Escort1st, OS, Chemo, TPS≥1%
		
Histogram of ln(HR) Escort1st, OS, Camre+Chemo, TPS≥1%	Histogram of |ln(HR)| Escort1st, OS, Camre+Chemo, TPS≥1%	Convergence plot Escort1st, OS, Camre+Chemo, TPS≥1%
		

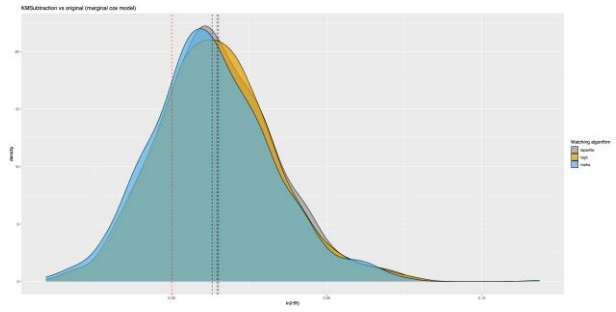
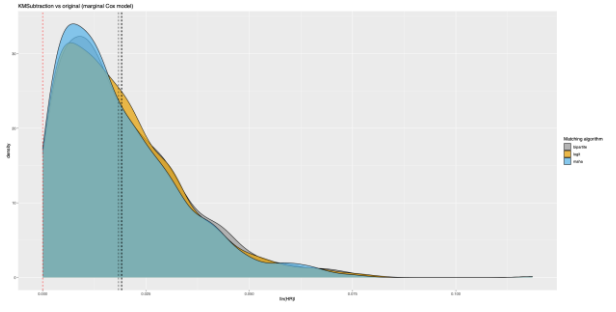
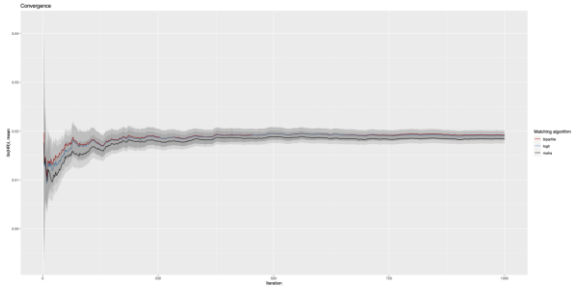
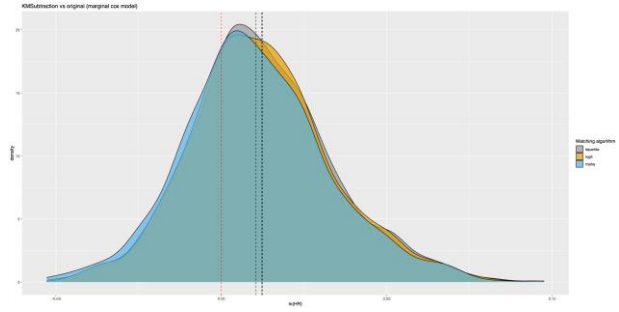
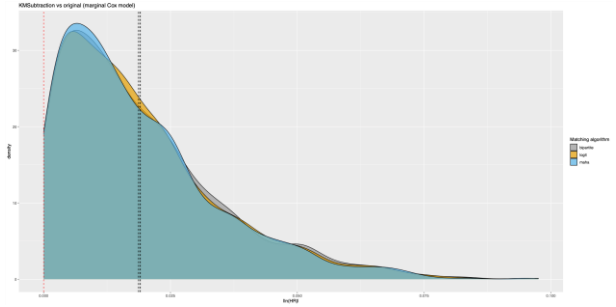
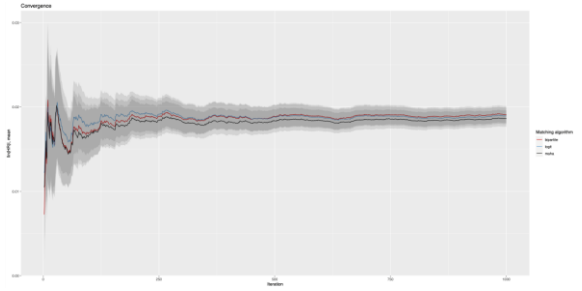
Histogram of ln(HR) KN181, OS, Chemo, CPS ≥10% 	Histogram of |ln(HR)| KN181, OS, Chemo, CPS ≥10% 	Convergence plot KN181, OS, Chemo, CPS ≥10% 
Histogram of ln(HR) KN181, OS, Pembro, CPS ≥10% 	Histogram of |ln(HR)| KN181, OS, Pembro, CPS ≥10% 	Convergence plot KN181, OS, Pembro, CPS ≥10% 

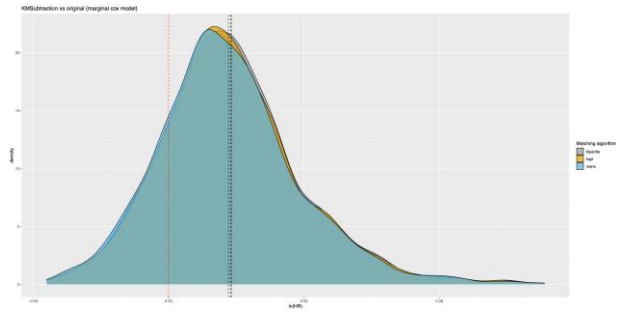
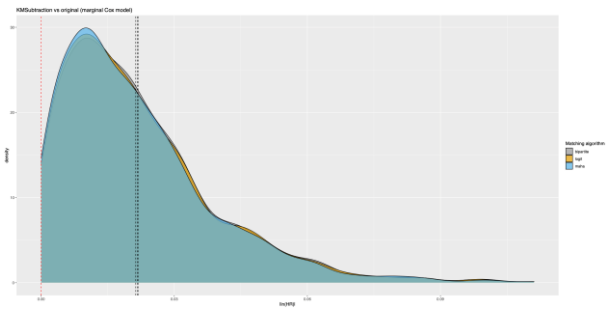
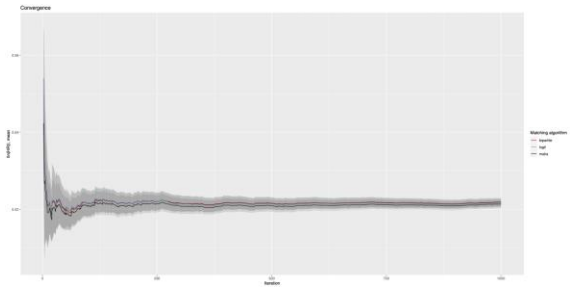
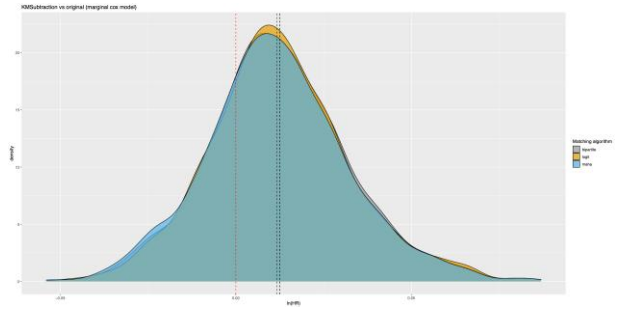
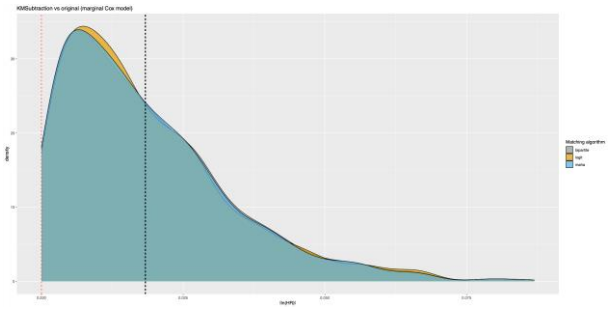
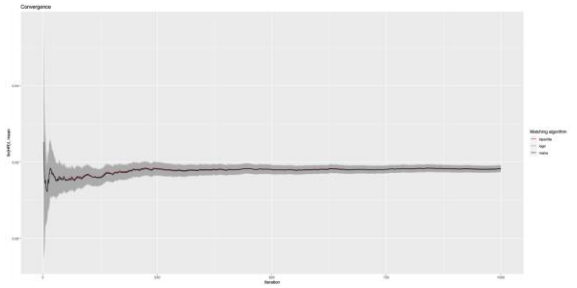
Histogram of ln(HR) Attraction3, OS, Chemo, TPS≥1%	Histogram of |ln(HR)| Attraction3, OS, Chemo, TPS≥1%	Convergence plot Attraction3, OS, Chemo, TPS≥1%
		
Histogram of ln(HR) Attraction3, OS, Nivo, TPS≥1%	Histogram of |ln(HR)| Attraction3, OS, Nivo, TPS≥1%	Convergence plot Attraction3, OS, Nivo, TPS≥1%
		

Histogram of ln(HR) KN590, OS, Chemo, CPS ≥10% 	Histogram of |ln(HR)| KN590, OS, Chemo, CPS ≥10% 	Convergence plot KN590, OS, Chemo, CPS ≥10% 
Histogram of ln(HR) KN590, OS, Pembro+Chemo, CPS ≥10% 	Histogram of |ln(HR)| KN590, OS, Pembro+Chemo, CPS ≥10% 	Convergence plot KN590, OS, Pembro+Chemo, CPS ≥10% 

Histogram of ln(HR) RATIONALE302, OS, Chemo, TAP ≥10% 	Histogram of |ln(HR)| RATIONALE302, OS, Chemo, TAP ≥10% 	Convergence plot RATIONALE302, OS, Chemo, TAP ≥10% 
Histogram of ln(HR) RATIONALE302, OS, Tisle, TAP ≥10% 	Histogram of |ln(HR)| RATIONALE302, OS, Tisle, TAP ≥10% 	Convergence plot RATIONALE302, OS, Tisle, TAP ≥10% 

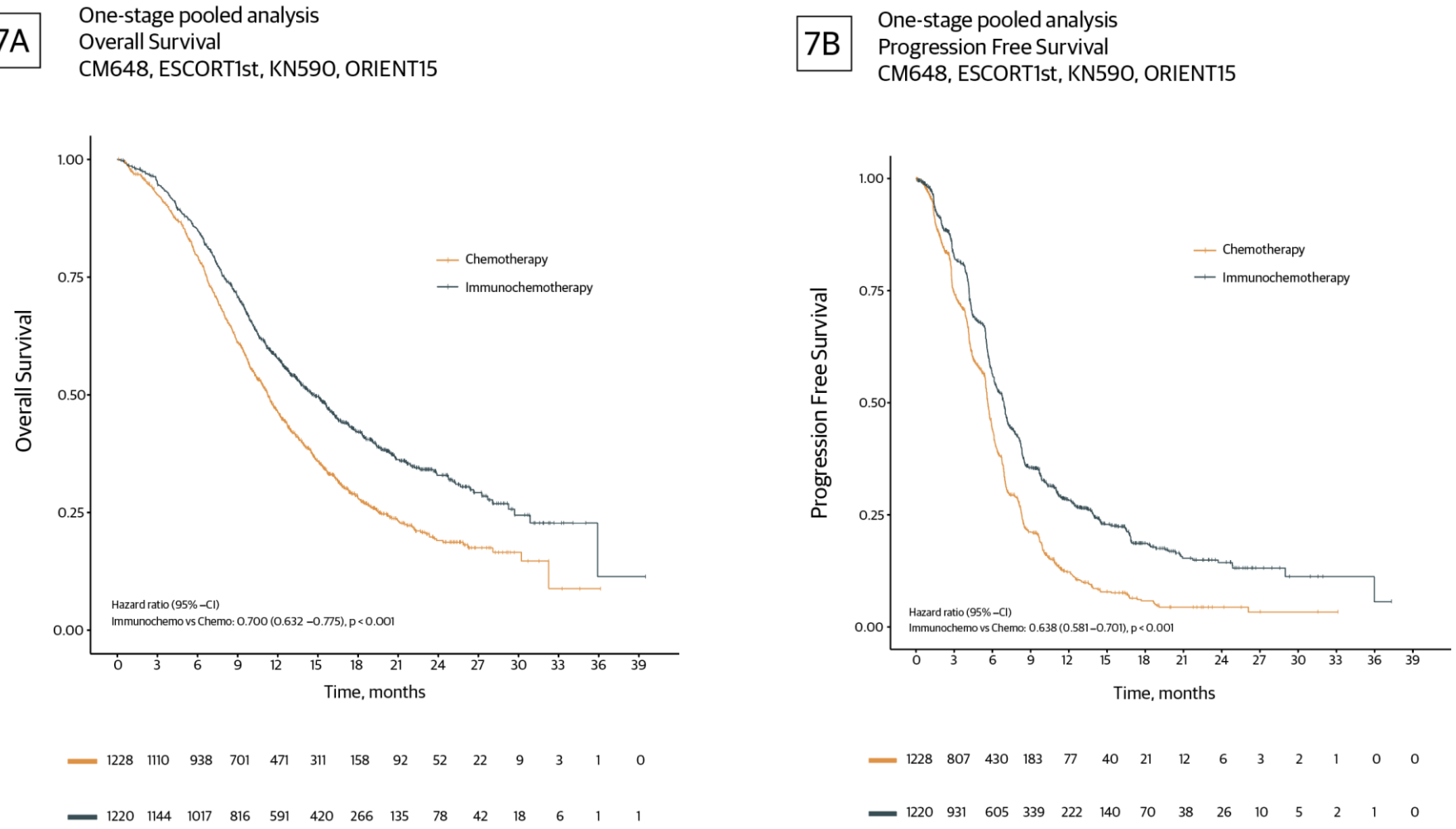
Histogram of ln(HR) ORIENT15, OS, Chemo, CPS ≥10% 	Histogram of |ln(HR)| ORIENT15, OS, Chemo, CPS ≥10% 	Convergence plot ORIENT15, OS, Chemo, CPS ≥10% 
Histogram of ln(HR) ORIENT15, OS, Sinti+Chemo, CPS ≥10% 	Histogram of |ln(HR)| ORIENT15, OS, Sinti+Chemo, CPS ≥10% 	Convergence plot ORIENT15, OS, Sinti+Chemo, CPS ≥10% 

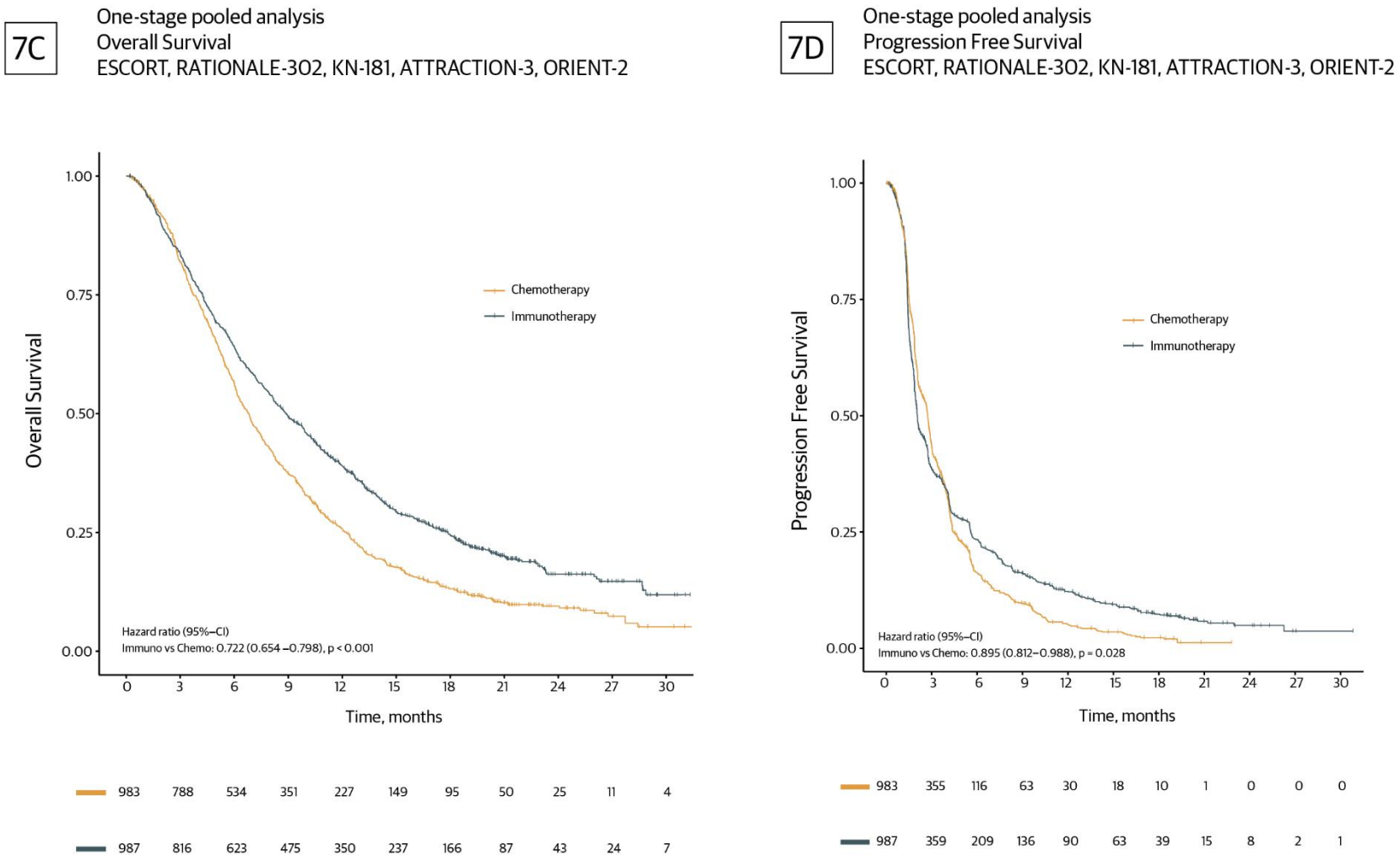
Histogram of ln(HR) ORIENT15, PFS, Chemo, CPS ≥10% 	Histogram of |ln(HR)| ORIENT15, PFS, Chemo, CPS ≥10% 	Convergence plot ORIENT15, PFS, Chemo, CPS ≥10% 
Histogram of ln(HR) ORIENT15, PFS, Sinti+Chemo, CPS ≥10% 	Histogram of |ln(HR)| ORIENT15, PFS, Sinti+Chemo, CPS ≥10% 	Convergence plot ORIENT15, PFS, Sinti+Chemo, CPS ≥10% 

Histogram of ln(HR) ESCORT, OS, Chemo, TPS ≥1%	Histogram of |ln(HR)| ESCORT, OS, Chemo, TPS ≥1%	Convergence plot ESCORT, OS, Chemo, TPS ≥1%
		
Histogram of ln(HR) ESCORT, OS, Camre, TPS ≥1%	Histogram of |ln(HR)| ESCORT, OS, Camre, TPS ≥1%	Convergence plot ESCORT, OS, Camre, TPS ≥1%
		

Convergence and histograms of simulations conducted for **eFigure 5** is demonstrated here. Abbreviations: Nivo, nivolumab; Ipi, ipilimumab; Camre, camrelizumab; Pembro, pembrolizumab; Sinti, sintilimab; Tisle, Tislelizumab; Chemo, chemotherapy; CPS, combined positive score; TPS, tumor proportion score; TAP, tumor area positivity; CM648, CheckMate 648; KN590, KEYNOTE-590; KN181, KEYNOTE-181.

eFigure 7. One-Stage Pooled Analysis of First-line and Second-line Studies





7(A) One stage meta-analyses of Overall Survival in first-line studies **(B)** One stage meta-analyses of Progression Free Survival in first-line studies **(C)** One stage meta-analyses of Overall Survival in second-line studies **(D)** One stage meta-analyses of Progression Free Survival in second-line studies