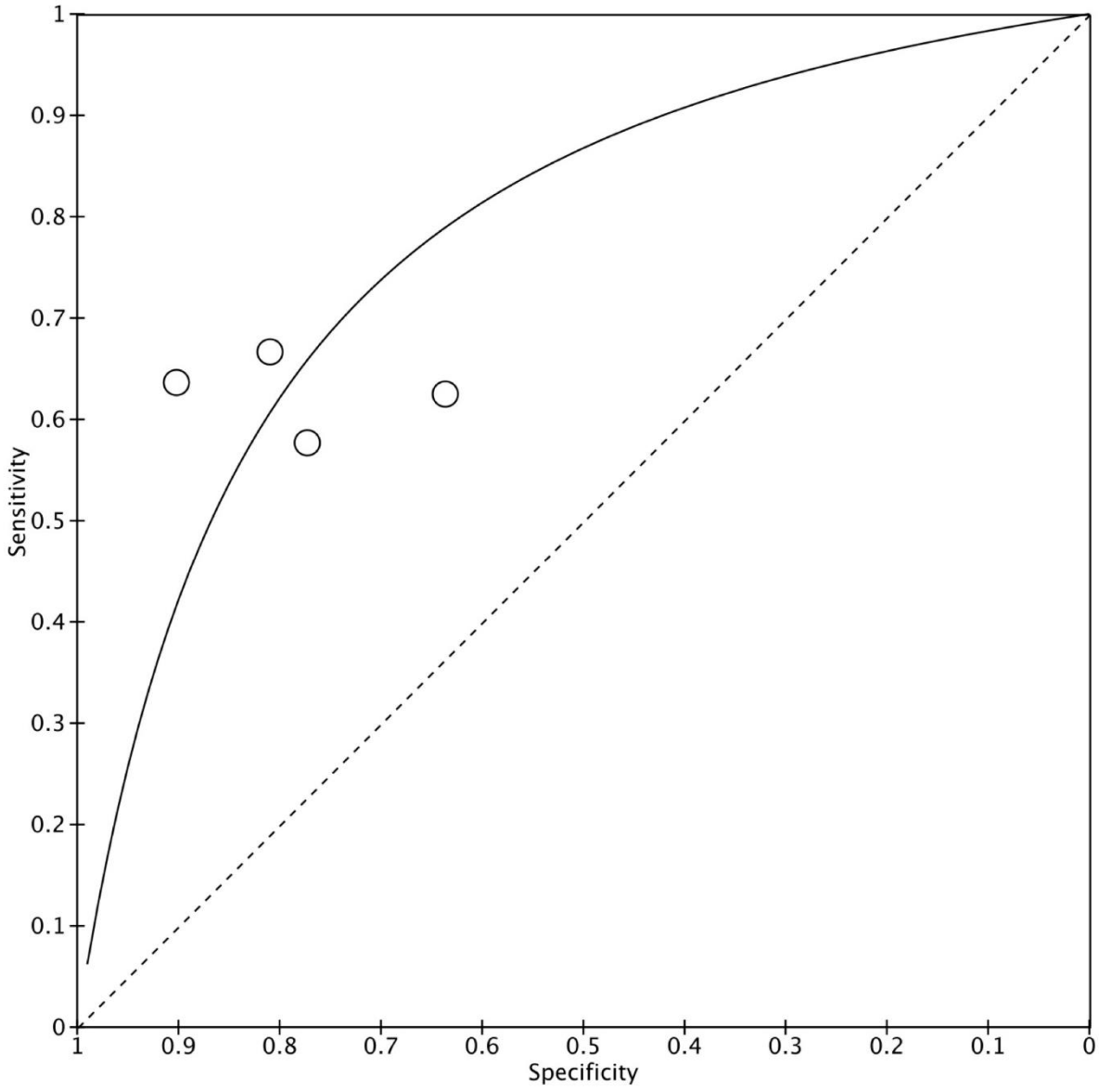
APPENDIX

Supplementary Figure 1. The summary receiver operating characteristic (ROC) curve



Supplementary Table 1. A summary of the articles that used computed tomography scan image data as input to machine learning

Author	Year	Study design	ML method	Patients in training set and validation	Neoadjuvant chemotherapy	Patients who Responders (%)	Sensitivity Specificity AUC	Year
Cha et al[12]	2016	Retrospective cohort	DL-CNN	62 patients/ 9 patients	MVAC	27%	AUC for predicting complete response (DL-CNN method): 0.73 +/- 0.06 AUC for predicting complete response (AI-CALS method): 0.70 +/- 0.06 AUC for predicting complete response (radiologist): 0.65+/- 0.07	2016
Cha et al[13]	2017	Retrospective cohort	DL-CNN and RAF classifier (SL/ROI)	82 patients/ 41 patients	MVAC (majority); while other patients were treated with regimens including Carboplatin, Paclitaxel, Gemcitabine, and Etoposide	22%	Sensitivity: DL-CNN=50%; RAF-SL= 50%; RAF-ROI=66.7%; Radiologist=91.7%. Specificity: DL-CNN=81%; RAF-SL=78.6%; RAF-ROI=54.8%; Radiologist=42.9% AUC: DL-CNN = 0.73 +/- 0.08; RAF-SL = 0.77 +/- 0.08;	2017

							RAF-ROI = 0.69 +/- 0.08; Radiologist = 0.77 +/- 0.07	
Wu et al[14]	2019	Retrospective cohort	DL-CNN	73 patients/ 50 patients	MVAC	33%	Specificity 80% to Sensitivity: Base structure (pretrained weights)=59,5%; Base structure (random weights)=41,7% DL-CNN1=50%; DL-CNN2=75%; DL-CNN3=50% Radiologist=0.77 +/- 0.08; RAF-SL=0.77 +/- 0.08; RAF-ROI - 0.69 +/- 0.08	2019
Cha et al[15]	2019	Retrospective cohort	DL-CNN and radiomics model	82 patients/ 123 patients	MVAC (majority); while other patients were treated with regimens including Carboplatin, Paclitaxel, Gemcitabine, and Etoposide	25%	AUC CDSS-T=0.80 +/- 0.04; Physicians= 0.74 [0.66-0.78]; Physicians + CDSS-T=0.77 [0.73-0.81] Easy Subset: CDSS-T=0.88; Physicians=0.81; Physicians + CDSS-T=0.84	2019

							Difficult Subset: CDSS-T=0.65; Physicians=0.59; Physicians + CDSS-T=0.62	
Hadjiiski et al[16]	2020	Retrospective cohort	DL-CNN and radiomics features	76 patients/ 123 patients	MVAC (majority); while other patients were treated with regimens including Carboplatin, Paclitaxel, Gemcitabine, and Etoposide. 3 cycles	25%	AUC: Interobserver variability CDSS-T=0.80 +/- 0.04; Physicians=0.74 +/- 0.04; Physicians + CDSS-T=0.77 +/- 0.04 Intraobserver variability: CDSS-T=0.85 +/- 0.06; Physicians= 0.78 [0.65-0.88]; Physicians + CDSS-T=0.81 [0.70-0.93]	2020
Choi et al[20]	2021	Retrospective cohort	RAF classifier	87 patients/ 48 patients	Specific NAC regimen not specified	40%	Imaging-based model: Training AUC: 0.85; 95% CI: 0.78 - 0.93 Validation AUC: 0.75; 95% CI: 0.60 - 0.86)	2021
Parmar et al[21]	2021	Retrospective cohort	RAF, SVM and SML	19 patients/ Validation: 19 patients with 10-fold nested cross-validation	Gemcitabine and Cisplatin: 18 patients MVAC: 1 patient	47%	Sensitivity: 52.9±9.4% Specificity: 69.4±8.6% Discriminative accuracy: 62.1±6.1%	2021

Sun et al[22]	2022	Retrospective cohort	RAF with modified leave-one-out cross-validation Elastic Net	82 patients / 123 patients	Specific NAC regimen not specified	25%	Average AUC Without CDSS-T=0.73 +/- 0.04; With CDSS-T=0.77 +/- 0.02 AUC for easy cancer subset: CDSS-T=0.88 Without CDSS-T=0.80; With CDSS-T=0.84 AUC for difficult cancer subset: CDSS-T=0.67 Without CDSS-T=0.58; With CDSS-T= 0.62	2022

CT: computed tomography, ML: machine learning, DL-CNN: Deep-learning convolutional neural networks, RAF: random forest, SL: segmented lesions, ROI: regions of interest, RBF: radial basis function, SVM: support vector machine, SML: supervised machine learning, MVAC: methotrexate vinblastine doxorubicin cisplatin, AUC: area under the curve, AI-CALS: auto-initialized cascaded level sets, CDSS-T: CT-based computerized decision-support system for muscle-invasive bladder cancer, CTU: CT urography

Supplementary Table 2. A summary of the articles that used genetic and anatomopathological data to train machine learning algorithms

Author	Year	Study design	Type of data	ML	Patients in training set	Patients in validation set	Neoadjuvant chemotherapy	Patients who Responders (%)	Sensitivity Specificity AUC
Mi et al[17]	2021	Retrospective cohort	Imaging of biopsy pathology specimens pre neoadjuvant treatment	SVM and RAF	66 patients	56 patients	At least 3 cycles of platinum / cisplatin-based chemotherapy	38%	ACC: 72.52 +/- 6.99% (best) AUC: 0.67 +/- 0.09% (best)
Hepburn et al[18]	2021	Retrospective cohort	Genetic data in machin learning (41 genes) versus Microarray differential gene expression analysis.	RGIFE and RAF	30 patients	99 patients	4 cycles of MVAC	63%	9-gene signature had 100% predictive accuracy in selecting responders from non-responders (CNGB1, GGH, HIST1H4F, IDO1, KIF5A, MRPL4, NCDN, PRRT3, SLC35B3)
Mohanad et al[19]	2021	Retrospective case-control	Epigenetic inactivation DDR genes (Retinoblastoma Bindi protein 8 and MutS homolog 4) associated with clinical features (tumor size, tumor grade, stage, lymph node, metastasis)	SVM, KNN, DT, LR and RFDT	80 patients	20 patients	Adjuvant and/or neoadjuvant cisplatin	-	The ROC curve prediction of response to therapy: AUC KNN: 0.96 RAF: 0.95 DT: 0.93 SVM: 0.93 LR: 0.92 The KNN in combination with RF and DT as detected by ensemble voting had an AUC of 0.96 Accuracy: 90.0±3.4% Sensitivity: 92.9% Specificity: 81.4%

NAC: Neoadjuvant chemotherapy, SVM: support vector machine, RAF: random forest, RGIFE: ranked-guided iterative feature elimination, DDR: DNA damage repair, KNN: K-nearest neighbor, DT: decision-tree, RFDT: random forest decision tree, LR: logistic regression, MIBC: muscle-invasive bladder cancer, PFS: progression-free survival, GC: gemcitabine and cisplatin, MVACdd: dose-dense methotrexate, vinblastine, doxorubicin and cisplatin.