

Table S1. Prospective clinical trials evaluating the effects of local anesthetics on cancer

NCT number	Phase, status	Local anesthetic (LA) injection	Administration route	Tumor type	Primary endpoint	Secondary endpoint
NCT03597087	NA, not yet recruiting	Bupivacaine vs GA	Spinal	Bladder	2-year recurrence-free survival	2-year cancer-free survival
NCT00938171	3, unknown	Lidocaine + bupivacaine+ sedation vs GA	Tumor site	Breast	Visual analog scale pain scores	PONV, opioid use, patient satisfaction, 5-year disease-free survival
NCT01204242	2, unknown	Lidocaine vs placebo	Intravenous	Breast	Opioid consumption	5-year recurrence Chronic pain
NCT00418457	3, completed	LA + propofol vs GA + opioids	Epidural or Regional	Breast	10-year recurrence	Postsurgical pain Neuropathic pain PCS/MCS score
NCT01716065	NA completed	LA vs GA	Regional	Breast	Circulating tumor cells	Level of cytokines/breast cancer antibodies/dendritic cells/T and B and natural killer lymphocytes
NCT04390698	NA, recruiting	Ropivacaine + GA vs lidocaine + opioid+ GA	Regional	Breast	Quality of recovery	Quality of life, postoperative pain, cancer recurrence up to 12 months
NCT03117894	NA, completed	Ropivacaine +GA vs GA	Regional	Breast	Opioid consumption, mortality	PONV, pain, 3- and 5-years recurrence
NCT01231204	4, completed	Ropivacaine vs placebo	Regional	Breast	Pain	Opioid use, sleep disturbance, 3-year cancer recurrence
NCT01916317	3, not yet recruiting	Lidocaine vs nothing	Tumor site	Breast	5-year disease-free survival	5-year overall survival
NCT04162535	1, recruiting	Lidocaine vs GA	Intravenous	Colo-rectal	Antiproliferative and apoptotic effects of anesthetic agents, evaluation of patient serum on colon cancer cell culture (HCT116)	Lidocaine concentration 5-year survival
NCT01318161	3, terminated	Ropivacaine vs opioid	Epidural	Colo-rectal	5-year mortality	7-year recurrence, inflammation (Perioperative cytokine concentration in blood), postoperative pain
NCT02012244	NA, completed	Ropivacaine vs opioid	Infiltration	Colo-rectal	NK cell activity, IL-2 level	1-year recurrence, inflammatory responses
NCT02786329	1, recruiting	Lidocaine+TIVA vs TIVA vs sevoflurane vs lidocaine+sevoflurane	Intravenous	Colo-rectal	5-year survival, 1- and 5-year recurrence	Opioid use, pain, bowel function, hospital stay
NCT04510935	NA, completed	Lidocaine vs GA	Sub-cutaneous	Liver	Percentage change from post- to pre-operative values of HepG2 cells invasion	Migration and proliferation of HepG2 cells cultured in patients' serum, serum IL-1 β , IL-6, TNF- α , IFN- γ and IL-2 level
NCT03594188	NA, completed	LA vs GA	Local	Liver	Cell proliferation	Cell migration and metastasis
NCT02474511	NA, unknown	LA vs GA	Local	Liver	Number of patients with tumor recurrence and metastasis after 3 years	NA

NCT03813953	NA, not yet recruiting	LA infiltration vs LA epidural	Infiltration vs epidural	Liver	5-year overall survival	3-year overall survival 5-year disease free survival
NCT02840227	NA, recruiting	LA+GA vs GA	Epidural	Lung	3-year cancer free survival	Pain, opioid use
NCT02801409	NA, completed	LA+GA vs GA	Epidural	Lung	4-year recurrence-free survival	Complications, ICU, chest tube, hospital stay, mortality, overall survival, pain, number of CD8+ and FOXP3+ T in tumor, percentage of NK-cells and T-cell in blood
NCT01179308	NA, terminated	LA+GA vs GA	Epidural	Lung	5-year disease-free survival	NK cell function, immune function markers, pain
NCT01588847	NA, unknown	Bupivacaine vs GA	Spinal	Melanoma	Overall survival	Change of total amount of Immune cells (T-, B-, NK-cells), changes in TGF- β , activation of thrombocytes, potential predictive biomarkers
NCT02256228	3, completed	Ropivacaine vs placebo	Intraperitoneal	Ovary	Inflammatory markers	Opioid use, pain, cognitive function, progression-free survival, morbidity
NCT04065009	3, recruiting	Ropivacaine vs placebo	Intraperitoneal	Ovary	Time to start of adjuvant chemotherapy after surgery	Complications, 3-5-year survival
NCT04048278	1, recruiting	Lidocaine vs placebo	Intravenous	Pancreas	Src tyrosine kinase activity in circulating tumor cells, cytokine/chemokine levels in serum, regulation of gene expression	Circulating tumor cells numeration
NCT04449289	2, not yet recruiting	Intravenous lidocaine +GA vs epidural ropivacaine +GA	Intravenous vs Epidural	Pancreas	1- and 3-year recurrence	1- and 3- year survival after surgery, LA concentration, complication
NCT03134430	NA, not yet recruiting	Ropivacaine + lidocaine vs placebo	Regional	Solid tumors	5-year cancer recurrence	5-year survival, percentage of immunocytes, content of cytokines, pain, recovery, hospital stay

GA, general anesthesia; ICU intensive care unit; LA, local anesthetics; NA, non-applicable; NK, natural killer; PCS/MCS, Physical and Mental Health Composite Scores; PONV, postoperative nausea and vomiting; TIVA, total intravenous anesthesia