

Supplementary 2

In vitro studies

Author	Year	Population	Intervention	Comparison	Outcomes
Law*	2022	Melanoma (B16 cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in B16 viability: 10% of controls at TXA 4%
		Melanoma (WM793 cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in WM793 viability: 10% of controls at TXA 4%
		Melanoma (MALME-3M cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in MALME-3M viability: 10% of controls at TXA 4%
		Breast tumor (MDA-MB-468 cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in MDA-MB-468 viability: 10% of controls at TXA 4%
		Breast tumor (MDA-MB-231 cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in MDA-MB-231 viability: 10% of controls at TXA 4%
		Breast tumor (BT474 cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in BT474 viability: Approx. 20% of controls at TXA 4%
		Breast tumor (HMEC cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in HMEC viability: 10% of controls at TXA 4%
		Breast tumor (MCF10A cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in MCF10A viability: 10% of controls at TXA 4%
		Prostate cancer (DU145 cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease in DU145 viability: ≤10% of controls at TXA 4%
		Neuroblastoma (SH-SY5Y cell line)	TXA 0-4%	TXA cultured Controls	Dose-dependent decrease SHS-SY5Y viability: ≤10% of controls at TXA 4%

		Multiple myeloma (KMS-18) cell line)	TXA 0-2%	TXA cultured Controls	Dose-dependent decrease in KMS-18 viability: Approx. 30% of controls at TXA 2%
		Multiple myeloma (KMS-11 cell line)	TXA 0-2%	TXA cultured Controls	Dose-dependent decrease in KMS-11 viability: Approx. 20% of controls at TXA 2%
		Multiple myeloma (JIM-3 cell line)	TXA 0-2%	TXA cultured Controls	Dose-dependent decrease in JIM-3 viability: Approx. 20% of controls at TXA 2%
		Chronic myelogenous leukemia (K562 cell line)	TXA 0-2%	TXA cultured Controls	Dose-dependent decrease K562 viability: Approx. 60% of controls at TXA 2%
		Acute lymphoblastic leukemia (MOLT4-S cell line)	TXA 0-2%	TXA cultured Controls	Dose-dependent decrease in MOLT4-S viability: Approx. 40% of controls at TXA 2%
		Lymphoma (4937 cell line)	TXA 0-2%	TXA cultured Controls	Dose-dependent decrease in 4937 viability: Approx. 40% of controls at TXA 2%
Esmaeili	2020	Glioblastoma cells (T98G & T98G-human-umbilical-vein-endothelial-cell (HUVEC) co-culture)	TXA 0.06, 0.6, 6, 12, 24, 48, 60 and 120 mM for 48 hours to investigate viability TXA 6 and 24 mM for 36 hours to investigate migration.	TXA exposed T98G culture TXA exposed T98G-HUVEC co-culture Control for T98G culture Control for T98G-HUVEC co-culture	TXA's effect on T98G culture - Viability: 65.32±6.26% of control at TXA concentration of 120 mM (p<0.001). - Migration: No difference in TXA-cultured T98G cells compared to controls. TXA's effect on T98G-HUVEC co-culture - Viability: 52.92±2.28% of controls at TXA concentration of 120 mM (p=0.000). - Migration: Reduced after 12 (p<0.01), 24 (p<0.01) and 36 (p<0.05) hours compared to controls.
Wu	2019	Human breast cancer (MDA-MB-231 BAG cell lines)	TXA 0.2-5 mM.	TXA culture Controls	Cell migration: 26±8.4% inhibition at 0.2 mM (p<0.005), 40±4.2% inhibition at 1mM (p<.0005) and no further reduction at 5 mM TXA.
		Ovarian adenocarcinoma (OVMZ6 cell lines)	TXA 0.2-5 mM.	TXA culture Controls	Cell migration: No difference compared to control.

Kaphle	2019	Glioma (U87 cell lines)	TXA 3 mM	TXA cultured TXA-collagen-hydrogel cultured Control cultured Control collagen-hydrogel-cultured	TXA cultured U87 compared to controls • Migration speed: 0.66 ± 0.20 $\mu\text{m}/\text{min}$ (NS). TXA-collagen-hydrogel cultured U87 • Migration speed: Inhibition with a speed of 0.55 ± 0.08 $\mu\text{m}/\text{min}$ compared to controls ($p < 0.05$). Migration speed of controls NR.
Suojanen	2009	Human tongue squamous cell carcinoma (HSC-3 cell lines)	TXA 6 mM for 48 h.	TXA culture Controls	• Viability: No effect of TXA. • Migration: Inhibition by $64 \pm 7\%$ ($p = 0.0016$). • Invasion: Inhibition by $36 \pm 13\%$ ($p = 0.036$).
		Human tongue squamous cells carcinoma (SCC-25 cell lines)	TXA 6 mM for 48 h.	TXA culture Controls	• Viability: No effect of TXA. • Migration: No effect of TXA. • Invasion: Inhibition by $52 \pm 5\%$ ($p = 0.0024$).
Wang	1996	Cholangiocarcinoma (QBC939 cell lines)	TXA or EACA at 50 c mg/L was added to a human amniotic membrane infiltration.	TXA culture EACA culture	TXA culture • Invasiveness: 4.20 ± 0.80 infiltrating cells compared to 12.10 ± 1.20 in controls ($p < 0.01$). EACA culture • Invasiveness: 4.80 ± 0.05 infiltrating cells compared to 12.80 ± 1.10 in controls ($p < 0.01$).
Kariko	1993	Human uroepithelial carcinoma (T24 cell lines)	TXA 1 mM for 40 min.	TXA culture Controls	• Invasiveness: Reduction by 96% ($p < 0.01$).
		Human uroepithelial carcinoma (J82 cell lines)	TXA 1 mM for 40 min.	TXA culture Controls	• Invasiveness: Reduction by 54% ($p < 0.05$).
		Human uroepithelial carcinoma (5637 cell lines)	TXA 1 mM for 40 min.	TXA culture Controls	• Invasiveness: Reduction by 50% ($p < 0.01$)
Kikuchi	1987	Serous cystadenocarcinoma of the ovary (HR cell lines)	TXA in different concentrations, NR	TXA cultured HR (doubling time 13.2 hours).	• Proliferation: 50% inhibition at 11.0 mg/ml TXA.
		Serous cystadenocarcinoma of the ovary (HR-1 cell lines)	TXA in different concentrations, NR	TXA cultured HR-1 cells (doubling time 17.6 hours).	• Proliferation: 50% inhibition at 10.8 mg/ml TXA.
		Serous cystadenocarcinoma of the ovary (HRA cell lines)	TXA in different concentrations, NR	TXA cultured HRA cells (doubling time 15.6 hours).	• Proliferation: 50% inhibition at 5.5. mg/ml TXA.
Kikuchi*	1986	Immature teratoma of the ovary (YK cell lines)	TXA 2.5, 5 and 10 mg/ml	TXA cultured Controls	• YK proliferation rate relative to controls: $95.5 \pm 15.9\%$ at 2.5 mg/ml, $71.3 \pm 12.3\%$ ($p < 0.01$) at 5.0 mg/ml and $69.4 \pm 9.7\%$ ($p < 0.01$) at 10.0 mg/ml TXA.

		Adenosquamous carcinoma of the ovary (NT cell lines)	TXA 2.5, 5 and 10 mg/ml	TXA cultured Controls	NT proliferation rate relative to controls: 98.7±13.9% at 2.5 mg/ml, 77.3±20.1% at 5 mg/ml and 49.5±10.6% (p<0.01) at 10.0 mg/ml TXA.
		Clear cell carcinoma of the ovary (OK cell lines)	TXA 2.5, 5 and 10 mg/ml	TXA cultured Controls	OK proliferation rate relative to controls: 122.3±22.8% at 2.5 mg/ml, 118.6±19.7% at 5.0 mg/ml and 108.6±11.3% at 10.0 mg/ml TXA. All findings nonsignificant.
		Serous cystadenocarcinoma of the ovary (HR cell lines)	TXA 2.5, 5 and 10 mg/ml	TXA cultured Controls	HR proliferation rate relative to controls: 89.3±14.7% at 2.5 mg/ml, 79.1±17.5% at 5.0 mg/ml and 69.4±9.7% (p<0.01) at 10.0 mg/ml TXA.
		Serous cystadenocarcinoma of the ovary (KK cell lines)	TXA 2.5, 5 and 10 mg/ml	TXA cultured Controls	KK proliferation rate relative to controls: 95.3±11.6% at 2.5 mg/ml, 63.4±7.5 (p<0.01) at 5.0 mg/ml and 63-1±9.7 (p<0.01) at 10.0 mg/ml TXA.
Kikuchi*	1986	Ovarian serous cystadenocarcinoma (HR cells derived from a patient with complete clinical response to TXA treatment)	TXA 32, 64, 256, 640 µM	TXA culture Controls	Proliferation rate compared to controls at different concentrations: 32 µM: Decreased by -21.4% 64 µM: Decreased by -36.3% 256 µM: Decreased by -37.7% 640 µM: Decreased by -39.5%
		Ovarian serous cystadenocarcinoma (KK cells derived from a patient with no clinical response to TXA treatment)	TXA 32, 64, 256, 640 µM	TXA culture Controls	Proliferation rate compared to controls at different concentrations: 32 µM: Increased by +24.8% 64 µM: Increased by +11.1% 256 µM: Increased by +10.0% 640 µM: Decreased by -1.1%
Ogawa*	1982	Lung squamous carcinoma (QG-56 cell lines)	TXA 1000, 100, 10 and 0 ug/ml.	TXA culture Controls	Viability: No effect of TXA
		Lung adenocarcinoma (PC-12 cell lines)	TXA 1000, 100, 10 and 0 ug/ml.	TXA cultured Controls	Viability: No effect of TXA
Iwakawa*	1982	Human lung cancer (PC9 cell lines)	TXA 1000 µg/ml	TXA cultured Controls	- PC 9 proliferation: No effects of TXA. - No. of cell reached 43.0±0.9 on day 7 compared to 42.7±1.2 in controls.
		Human renal pelvic cancer (KP1 cell lines)	TXA 1000 µg/ml	TXA cultured Controls	- KP1 proliferation: No effects of TXA. - No. of cell reached 16.9±0.9 on day 7 compared to 17.1±1.0 in controls.

Sekiya	1980	Ovarian adenocarcinoma (ROT58/C3 cell lines)	Increasing concentrations.	TXA culture EACA culture Controls	TXA culture - Colony forming rate: Concentrations at 10 to 100 µg/ml promoted the colony forming rate, but higher concentrations at 1000 µg/ml reduced rates by 40%. EACA culture - Colony forming rate: Dose-dependent reduction up to 70% at 1000 µg/ml.
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Animal studies

Author	Year	Population	Intervention	Comparison and sample size	Outcomes
Hiramoto	2022	Specific-pathogen-free female mice with endometrial cancer induced by N-methyl-N-nitrosourea (MNU) and estradiol.	TXA P.O. 12 mg/kg three times weekly for 30 weeks. Control intervention: Distilled water.	TXA treatment + endometrial cancer (n=10) Control intervention + endometrial cancer (n=10) Control intervention (n=10)	TXA treatment group: - Uterus weight reduction (p<0.05) - Total body weight (NS) - Ki67 reduction (p<0.05) - CA125 reduction (p<0.05)
Law*	2022	NOD-SCID-gamma (NSG) mice inoculated with 012/LVM2/LR10 breast tumor cell line	TXA P.O. 375 mg/kg for 12 days Control intervention: Peanut oil	TXA treatment group (n=5) Controls (n=5)	TXA treatment group: Reduced tumor volume 9.3 mm³ vs. 81.7 mm³ (p=0.035).
		NOD-SCID-gamma (NSG) mice inoculated with 012/LVM2/LR10 breast tumor cell line	TXA P.O. 375 mg/kg for 20 days Control intervention: Peanut oil	TXA treatment group (n=10) Controls (n=10)	TXA treatment group: Reduced tumor volume <50 mm³ vs. >200 mm³ (p-value, NA).

Hiramoto	2019	Hairless, male, specific-pathogen-free mice with 7,12-Dimethylbenz(a)anthracene (DMBA) and UVA-induced non-melanoma skin cancer.	TXA P.O. 750 mg kg ⁻¹ three times weekly for 15 weeks + DMBA TXA P.O. 750 mg kg ⁻¹ three times weekly for 15 weeks + DMBA + UVA DMBA + UVA Control intervention: Distilled water.	a. TXA + DMBA treatment group (n=5) b. TXA + DMBA + UVA treatment group (n=5) c. DMBA + UVA treatment group (n=5) d. Controls (n=5)	TXA treatment groups: - No. of tumors was 0 in TXA-treated (group a) compared to 0 in controls (group d) (NS). - No. of tumors was approx. 4 in TXA-treated (group b) compared to 7.5 in non-TXA-treated (group c) (p<0.05). - Area per tumor was 7.5 mm² in TXA-treated (group b) compared to 17.5 mm² non-TXA-treated (group c) (p<0.05).
Yamamoto	2017	Male KSN/slc mice implanted S.C. with lung carcinoma SBC-3A cells.	TXA I.P. 30 mg daily for 10 days. Control intervention: NR.	TXA treatment group (n=4) Controls (n=4)	TXA treatment group: Tumor growth reduced by 30% (p<0.05).
Garona	2014	BALB/c mice inoculated I.V. with mammary carcinoma (F3II) cells.	TXA I.V. 10 mg/kg at inoculation TXA I.V. 10 mg/kg at inoculation + 24 hours after inoculation Control intervention: NR	TXA 0 hours (n, NR) TXA 0 hours + 24 hours (n, NR) Controls (n, NR)	No difference in the formation of lung metastases between the three intervention groups.
Kirstein	2008	Female mice (C57B1/6) inoculated I.V. with melanoma (B16F10) cells.	EACA I.V. 60 mg in 100 µl volume 15 minutes before inoculation. Control intervention: Saline 100 µl.	EACA treatment group (n=10-16) Control (n=10-16)	EACA treatment group: Increased number of lung metastases (p<0.05).
Horiguchi	2000	Female Syrian Goldso hamsters with n-nitrosobis(2-hydroxypropyl)amine-induced pancreatic ducts carcinoma.	TXA P.O. 0.1% daily 50 days after induction until euthanasia on day 88. Control intervention: Untreated.	TXA treatment group (n=20) Control (n=20)	TXA treatment group: - Mortality: 2 vs. 3 animals died (ns) - Reduced incidence: 22% vs. 59% (p<0.05) - Decreased no. of carcinoma lesions: 0.27±0.57 vs. 0.88±0.78 (p<0.05)
Wanaka	1996	Mice inoculated I.P. with sarcoma (-180) cells	TXA S.C. 2000 mg/kg daily for 5 days Control intervention: NR.	TXA treatment groups (n, NR) Controls (n, NR)	TXA treatment group: - Decreased ascitic volume (p<0.05). - Decreased tumor cell number (p<0.05).

Shinkfield	1992	BALB/c mice inoculated I.P. squamous cell carcinoma (A431) cells.	TXA I.P. 1.5 mg in 0.5 ml saline daily from the day after inoculation until day 18. Control intervention: Saline	TXA treatment group (n, NR) Controls (n, NR)	Treatment with TXA did not affect tumor growth.
Sawaya	1986	BALB/c mice implanted S.C. with fresh glioblastoma tumor obtained from patients undergoing surgery.	EACA P.O. 2.5 mg in 100 ml sterile water EACA P.O. 5 mg in 100 ml sterile water Control intervention: Benzyl alcohol 0.9%.	EACA 2.5% treatment group (n=10) EACA 5% treatment group (n=12) Controls (n=10)	EACA 2.5% treatment group vs. controls: - Reduced tumor growth rate: 0.55 mm³/day vs. 0.81 mm³/day (p<0.05). - Reduced tumor volume at death: 8.47 mm³ vs. 9.04 mm³ (ns.) - Increased survival: 49.5 days vs. 34.5 (p<0.05). EACA 5% treatment group vs. controls: - Reduced tumor volume at death: 7.85 mm³ vs. 9.04 mm³ (p<0.05). EACA 2.5% vs. EACA 5%: - Increasing the dose had no significant effect on tumor growth rates or survival.
Shibata	1986	CH3 mice with I.P. inoculated ascites tumor with breast carcinoma (MM2) cells.	TXA I.P. 1200 mg/ml daily from day 1-12. Control intervention: Saline: 0.2-0.4 ml	TXA treatment group (n=17) Control group (n=24)	TXA treatment group: - Reduced weight gain rate: 125.8±1.6% vs. 133.2±4.0% on day ten (p<0.001). - Reduced ascitic fluid: 8.8±1.6ml vs. 11.6±2.4ml on day 12 (p<0.05). - Reduced tumor cell ratio in ascites: 22.3 ± 1.7% vs. 28.8± 3.0% on day eight (p<0.001). - Reduced tumor cell ratio on day 10 14.3±4.5% vs. 21.6±5.2% (p<0.05). - Reduced tumor cell ratio on day 12 11.8±2.7% vs. 16.0±3.0% (p<0.05).
Kikuchi*	1986	Nude female BALB/c mice inoculated S.C. with TXA-exposed or non-TXA-exposed ovarian tumor (HR) cell line.	TXA 10mg/ml in culture for 2 hours prior to inoculation.	TXA-exposed-cell tumor group (n=10) Unexposed-cell tumor group (n=10)	TXA treatment group: - No difference on Days 14, 21, and 28 - Decreased tumor volume at Day 36: 1.26 ±0.60 cm³ vs. 2.78±0.76 cm³ (p<0.01) - Decreased tumor volume at Day 43: 2.57 ±1.39 cm³ vs. 4.96 ±1.56 cm³ (p<0.01)

Conforti	1984	C57 B1/6 mice implanted I.M. with Lewis lung carcinoma (3LL) cells.	TXA P.O. 0.5 g/kg daily for 18 days. TXA P.O. 1 g/kg daily for 18 days. TXA P.O. 2 g/kg daily for 18 days.	TXA 0.5 g treatment group (n, NR) TXA 1 g treatment group (n, NR) TXA 2 g treatment group (n, NR)	- Lung metastase weight tended to increase in the two higher doses. - Mean survival time, primary tumor weight, and number of lung metastases showed no difference between the three intervention groups.
Tanaka	1982	Female BDF1 mice (C57BL/6 x DBA/2) inoculated S.C. with Lewis Lung carcinoma.	TXA P.O 3 g/kg. daily from one day before inoculation until amputation on day 12. Control intervention: Untreated.	TXA treatment group (n=10) Controls (n=10)	TXA treatment group: Reduced number of pulmonary metastatic foci: 7.0±1.9 (SE) vs. 21.2±2.5 (SE) (p<0.05).
Ogawa*	1982	Female, nude mice (BALB/cAnu/nwJCL) inoculated S.C. with lung squamous carcinoma (QG-56) cells.	TXA P.O. 1% Control: Untreated	TXA treatment group (n=11) Controls (n=10)	TXA treatment group: - Reduced tumor weight 1.23±0.10 (SE) g vs. 0.81±0.11 (SE) g (p<0.01). - Increased tumor border fibrin deposition from moderate to severe.
		Female, nude mice (BALB/cAnu/nwJCL) inoculated S.C. with lung adenocarcinoma (PC-12) cells.	TXA P.O. 1% Control: Untreated	TXA treatment group (n=11) Controls (n=10)	TXA treatment group: - Reduced tumor weight 1.30±0.16 (SE) g vs. 0.81±0.11 (SE) g (p<0.05). - Increased tumor border fibrin deposition from slight to moderate.
		Female, nude mice (BALB/cAnu/nwJCL) inoculated S.C. with ovarian carcinoma (OC-1) cells.	TXA P.O. 1% Control: Untreated	TXA treatment group (n=11) Controls (n=10)	TXA treatment group: - Reduced tumor weight 2.03±0.26 (SE) g vs. 1.21±0.18 (SE) g (p<0.01). - Increased tumor border fibrin deposition from slight to moderate.
Iwakawa*	1982	Nude BALB/c mice inoculated S.C. with human lung cancer (PC9) cell line.	TXA P.O. 1% Control: Untreated	TXA treatment group (n=8) Controls (n=8)	Treatment with TXA did not affect tumor weight (tumor weight relative to control: 82.8% (ns).
		Nude BALB/c mice transplanted with human ovarian cancer (OC1) tumor.	TXA P.O. 1% Control: Untreated	TXA treatment group (n=7) Controls (n=6)	Treatment with TXA did not affect tumor weight (tumor weight relative to control: 65.8% (ns).

		Nude BALB/c mice transplanted with human renal pelvic cancer (NKPP1) tumor.	TXA P.O. 1%	TXA treatment group (n=8) Controls (n=7)	Treatment with TXA did not affect tumor weight (tumor weight relative to control: 70.1% (ns).
Sundbeck	1981	Lister strain rats transplanted I.M. with a 20-methylcholanthrene-induced sarcoma (128th to 130th transfer generations).	TXA 200 mg/100g bw once daily Control intervention: NR.	TXA, early treatment (day 1-7) (n=8) TXA, late treatment (day 8-14) (n=8) Controls (n=8)	TXA treatment group: - Reduced tumor weight during early treatment 6.0±3.2g vs. 11.9±2.3g (p<0.05). - Reduced tumor weight during late treatment 6.6±1.6g vs. 11.9±2.3 (p<0.05).
Sundbeck	1981	Lister strain rats transplanted with a 20-methylcholanthrene-induced sarcoma (122nd transfer generations).	TXA 200 mg/100g bw, I.P., once daily for 10 days. Control intervention: NR.	TXA treatment group (n=11) Controls (n=11)	TXA treatment group: Reduced tumor weight 7.7±0.7 (SE) g vs. 10.9±0.5 (SE) g (p<0.05).

Kodama ⁵³	1981	New Zealand white male rabbits implanted I.M. with V2 carcinoma cells.	TXA P.O. 500 mg/kg. Control intervention: Untreated.	TXA 1-week-treatment group (n=10) Controls 1-week-treatment (n=10) TXA 2-week-treatment group (n=8) Controls 2-week-treatment (n=8) TXA 3-week-treatment group (n=17) Controls 3-week-treatment (n=18)	TXA 1-week-treatment group: - No difference in tumor weight 0.3±0.1 vs. 0.3±0.1 (ns). - No difference in metastatic incidence (Popliteal node): 9/10 vs. 8/10. - Reduced number of metastatic foci 1.4±1.0 vs. 3.8±2.9 (p<0.05). TXA 2-week-treatment group: - Reduced tumor weight 6.6±3.4 vs. 10.0±3.7 (p<0.1). - Reduced metastatic incidence (Popliteal node) 5/8 vs. 8/8. - Reduced lung metastases 1/8 vs. 3/8. TXA 3-week-treatment group - Reduced tumor weight: 13.9±9.8 vs. 23.4±18.4 (p<0.1). - Reduced metastasis incidence (p<0.1): Popliteal metastases 9/17 vs. 12/18 Pelvic metastases 2/17 vs. 6/18 Lung metastases 7/17 vs. 12/18 - Reduced no. of metastatic lung foci 2.8±4.1 vs. 19.9±34.2 (p<0.1).
Astedt ⁵⁴	1980	C57 mice inoculated S.C. with Lewis lung adenocarcinoma cells.	TXA P.O. 0.5 g/kg daily for 10 days. Control intervention, NR.	TXA treatment group (n=10) Controls (n=10)	TXA Treatment group: - Demarcated, smaller, and non-ulcerated tumors - Reduced mean survival 35±2 days vs. 28±2 days
		C3H mice inoculated S.C. with breast carcinoma cells.	TXA P.O. 0.1 g/kg daily for 20 days. Control intervention, NR.	TXA treatment group (n=10) Controls (n=10)	TXA Treatment group: Tumor weight 1.76±0.07 g compared with 2.01±0.08 g in controls
		Sprague-Dawley rats inoculated S.C. with hepatoma cells.	TXA P.O. or I.P. 0.5 g/kg daily for 10 days. Control intervention, NR.	TXA treatment group (n=10) Controls (n=10)	TXA P.O. treatment group: - Ascitic fluid 24±4.0 ml compared to 52±6.0 ml in controls TXA I.P. treatment group: - Ascitic fluid 46±5.2 ml compared to 82±4.7 ml in controls.

Peterson ⁵⁵	1976	Lister strain rats injected I.M. with blood from an operatively treated 20-methylcholanthrene-induced sarcoma tumor.	TXA P.O. 3% concentration in the drinking water for 3 days before tumor excision. Control intervention, NR	TXA treatment group (n=15) Controls (n=15)	- Tumor incidence: 7/15 in both TXA-treated animals and controls - Tumor weight: 26.5±16.7 in TXA-treated animals compared to 25.1±16.7 in controls.
		Lister strain rats injected I.M. with blood from an operatively treated 20-methylcholanthrene-induced sarcoma tumor.	TXA I.V: 100 mg 2 hours and immediately before tumor excision. Control intervention, NR	TXA treatment group (n=15) Controls (n=15)	- Tumor incidence: 5/15 in the TXA-treated animals compared to 4/15 in controls. - Tumor weight: 15.2±17.1 in the TXA-treated animals compared to 36.1±29.7 in controls.
		Lister strain rats injected I.M. with blood from an biopsy-treated 20-methylcholanthrene-induced sarcoma tumor.	TXA I.V: 100 mg 2 hours and immediately before tumor excision. Control intervention, NR	TXA treatment group (n=15) Controls (n=15)	- Tumor incidence: 8/15 in the TXA-treated animals compared to 5/15 in controls - Tumor weight: 10.7±8.0 in the TXA-treated animals compared to 19.2±15.6 in controls
		Lister strain rats injected I.V. with blood from an operatively treated 20-methylcholanthrene-induced sarcoma tumor.	TXA I.V: 100 mg 2 hours and immediately before tumor excision. Control intervention, NR	TXA treatment group (n=8) Controls (n=8)	Tumor incidence: 2/8 in the TXA group compared to 0/8 in the controls.
Boeryd ⁵⁶	1974	C57BL/6J mice inoculated I.V. with melanoma (B16) cells.	TXA I.P. 12 mg in a single dose 30 minutes before inoculation.	TXA treatment group (n=30)	TXA treatment group: - Increased no. of lung metastases 121 vs. 82 in controls (p<0.05). - Increased avg. volume of lung metastases 291 10⁻⁶ cm³ vs. 153 10⁻⁶ cm³ (p<0.05). - Increased total volume of lung metastases 34 10⁻³ cm³ vs. 13 10⁻³ cm³ (p<0.05). EACA treatment group: - No difference in no. of lung metastases 82 compared to 82 in controls (NS). - Increased avg. volume of lung metastases 230 10⁻⁶ cm³ vs. 153 10⁻⁶ cm³ (p<0.05). - Increased total volume of lung metastases 19 10⁻³ cm³ vs. 13 10⁻³ cm³ (p<0.10).
			EACA I.P. 60 mg in a single dose 30 minutes before inoculation.	EACA treatment group (n=30)	
			Control intervention: Saline 0.2 ml.	Controls (n=32)	

CBA mice inoculated I.V. with sarcoma (MCG1-SS) cells.	TXA I.P. 12 mg in a single dose 30 minutes before inoculation.	TXA treatment group (n=20)	TXA treatment group vs. controls:
EACA I.P. 60 mg in a single dose 30 minutes before inoculation.	EACA I.P. 60 mg in a single dose 30 minutes before inoculation.	EACA treatment group (n=20)	EACA treatment group vs. controls:
Control intervention: Saline 0.2 ml.	Control intervention: Saline 0.2 ml.	Controls (n=20)	Controls
Hisazumi ⁵⁷	1973	Male Wistar rats with N-butyl-N-butanol(4)-nitrosamine (BBN)-induced bladder tumors.	TXA P.O. 0.05 M for 30 days.
Control intervention: Untreated.	Control intervention: Untreated.	TXA treatment group (n=10)	TXA treatment group compared to controls:
TXA treatment + BBN (n=10)	TXA treatment + BBN (n=10)	TXA treatment + BBN (n=10)	TXA + BBN treatment group compared to BBN group:
BBN + control intervention (n=10)	BBN + control intervention (n=10)	BBN + control intervention (n=10)	BBN + control intervention
Control intervention (n=10)	Control intervention (n=10)	Control intervention (n=10)	Control intervention

Clinical studies

Author	Year	Population	Intervention	Comparison and sample size	Outcomes
Kikuchi ^{35*}	1986	Patients with advanced proven ovarian carcinoma (serous cystadenocarcinoma, mucinous cystadenocarcinoma, clear cell carcinoma), FIGO stage III-IV and with cytologically proven malignant ascites and previously exposed to mono chemotherapy. Age 42-69 years.	TXA 4 g I.P. daily for 2 weeks. Chemotherapy was given one week after treatment with TXA.	TXA treatment (n=11)	TXA treatment response evaluated by ascitic fluid volume and detection of tumor cells. Complete response was defined as complete ascitic fluid regression and tumor cell elimination. Partial response was defined as reduction in ascitic fluid and tumor cell elimination. Response • Complete response: 4/11 (36.4%) patients • Partial response: 2/11 (18.2%) patients • No change: 5/11 (45.5%) patients Patients with no clinical response had poorly differentiated tumors in 4/5 cases compared to 2/6 in the patients with response. Survival: 12 months in patients responding to TXA treatment compared to 5 months in patients not responding to TXA treatment.
Petrelli ⁶²	1986	Seven patients had an inadequate trial because of toxic effects and were not evaluated for outcome. One patient died within 4 weeks of treatment from hepatic failure, secondary to metastases. Twelve patients had an adequate trial. Three patients had stable disease Nine had progression.	Seven patients had an inadequate trial because of toxic effects and were not evaluated for outcome. One patient died within 4 weeks of treatment from hepatic failure, secondary to metastases. Twelve patients had an adequate trial. Three patients had stable disease Nine had progression.	Seven patients had an inadequate trial because of toxic effects and were not evaluated for outcome. One patient died within 4 weeks of treatment from hepatic failure, secondary to metastases. Twelve patients had an adequate trial. Three patients had stable disease Nine had progression.	Seven patients had an inadequate trial because of toxic effects and were not evaluated for outcome. One patient died within 4 weeks of treatment from hepatic failure, secondary to metastases. Twelve patients had an adequate trial. Three patients had stable disease Nine had progression.

Sigurdsson ⁵⁸	1983	Patients with recurrent ovarian carcinoma (FIGO Stage IIb, III and IV) resistant to chemotherapy.	Cyklokapron 4-6 g P.O. daily. Patients with an objective response or stable disease continued treatment until progression.	Complete remission: the complete disappearance of all measurable lesions for at least three months	Prior to TXA treatment, two patient received chemotherapy, and the remaining 24 patients received both chemo- and radiotherapy.
		Total n = 26		Partial remission: a 50% reduction at least of measurable tumor, with no pleural or ascitic fluids persisting	Five patients had stable disease, median duration was six (range 3-34) months, median survival of 12.5 (range 4-36) months.
				Stable disease: 0-49% decrease in measurable tumor volume and no new lesions or improvements	21 patients showed within three months and a median survival of four months
				Progressive disease: An increasing volume of tumor or new lesions during treatment without remission or shortening of the intervals between paracenteses, relapse after remission, a new lesion or recurrence in a previously regressed area.	All 21 patients with progression had poorly differentiated tumors on histology, whereas the five patients with stable disease had highly and moderately differentiated tumors.
Soma ⁵⁹	1980	Ovarian cancer, Stage IV. Case of inoperable ovarian cancer in a 60-year-old woman resistant to radiotherapy and chemotherapy hospitalized for accumulation of ascitic fluid.	TXA given in a dose of 1.5-2.0 g three times a day every day, sometimes augmented by TXA 3-5g I.P. or I.V.	NA	After three months of TXA treatment, the production of ascitic fluid regressed, and repeated paracentesis was no longer necessary.
		Total n = 1			Exploratory laparotomy showed a thickened peritoneum with an encapsulated ovarian tumor. Microscopic assessment of the tumor confirmed that it was a metastasis encapsulated by proliferative connective tissue and fibrinoid degeneration with fibrinolytic activity.
					Five months after admission, the patient is still free from symptoms and continues treatment with TXA.

Bramsen ⁶³	1978	Patients with choroidal melanoma.	Patient a) Cyklokapron 0.75 g 4 times daily for 6 months.	Visual acuity, tumor size and visual field on perimetry for patient a.	Patient a) Visual acuity was <0.33 -2.5 sphere, and after six months of treatment, visual acuity was > 0.2 -3.0 sphere. Tumor size on ophthalmoscopy and visual field on perimetry were both unchanged.
		Patient a) 39-year-old male Patient b) 51-year-old male Patient c) 39-year-old female Patient d) 67-year-old male Total n = 4	Patient b) Cyklokapron 0.75 g 4 times daily for 5 months. Patient c) Cyklokapron 1.5 g 3 times daily for 5 days. Patient d) Cyklokapron 1.5 g 3 times daily for 3 days. Administration route NR.	The remaining patients underwent enucleation and pathohistological examination.	Patients b, c and d) Histopathological examination showed fibrin-rich deposits surrounding all tumors. The degree of fibrin deposition increased with longer treatment periods.
Fosså ⁶⁰	1978	Patients with advanced cancer and metastases to bone, liver, lungs, pleura and skin.	Cyklokapron 1-5 g P.O. daily for 4 to 17 weeks.	Clinical response and adverse events in TXA treatment.	Of the 19 patients, 15 had previously been treated with long-term chemotherapy without effects before treatment with TXA. Previous treatment was discontinued except in one patient where the treatment was changed. This patient received cytostatic therapy in combination with TXA, along with the remaining four patients.
		Cancer renis (n =3), Mammae (n = 6) Vesicae (n = 1) Sublingualis (n = 1) Coli (n = 5), Testis (n = 1) Melanoma (n = 2) Total n = 19		Clinical response was defined as: Complete remission: Complete remission in all symptoms and clinical findings. Partial remission: At least 50% remission of all quantifiable symptoms and clinical findings. Stable disease: No increase in symptoms or clinical findings. Progression: Increased of the number or intensity of symptoms and clinical findings.	Clinical response: 18 patients showed progression. One patient had stable disease. Adverse events and side effects: Gastrointestinal symptoms were recorded in four patients, and one patient developed a deep vein thrombosis.

Rutqvist ⁶¹	1977	Patients with advanced cancer. Breast cancer (n=5) Ovarian cancer (n=2) Melanoma (n=1) Ewing sarcoma (n=1) Adenocarcinoma with unknown primary location (n=1) Total n = 10	Cyklokapron 1 g P.O. 2-3 times daily for 3-10 weeks. The dosage was reduced to 0.5 g in two patients due to gastrointestinal side effects.	Clinical effect	All patients had previously cytostatic treatment while six patients continued with concurrent treatment with TXA and cytostatic. The five patients with advanced breast cancer had both improvement and decline in clinical status. The two patients with advanced ovarian cancer had no clinical change The patient with advanced melanoma had no clinical changes. The patient with Ewing's sarcoma had progression in pulmonary metastases. The patient with advanced adenocarcinoma of unknown origin had an increase in tumor size.
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Included studies: Studies included in the review listed according to study categories in vitro, animal, or clinical study and year of study. Studies marked * are listed several times reporting findings across study categories. Findings are reported as mean±sd unless otherwise specified. P.O. = Per OS, I.V.= Intravenous, I.P. = Intraperitoneal, BW = Body weight, TXA = tranexamic acid, EACA = Epsilon-amniocapronic acid, NA = not applicable, NR= Not reported, SE = Standard error, Approx.=Approximately, No.= Number, bw = body weight.