Supplementary

Table S1 Antibody trials in pancreatic cancer

Trial (year)	Phase	#pts	Target	Agent	Stage	1st/2nd line	Other Tx	Median OS	Result	Comment
Xiong (2004)(86)	II	41	EGFR	Cetuximab	LAPC, M1	1st	Gem	7.1 mo	1-year OS 31% PR 12%, SD 63%	intratumoral EGFR expression
Van Cutsem (2009)(87)	III RCT	607	EGFR, VEGF-A	Erlotinib +Bevacizumab	M1	1st	Gem	7.1 *vs.* 6 mo	No benefit	1.Gem+Erl+Bev 2.Gem+Erl+placebo
Fujisaka (2015)(164)	I	17	mesothelin	amatuximab	nr	2nd+	no	nr	3 with SD	Mixed solid tumors Mesothelin-positive Tu on IHC
Fuchs (2015)(97)	III RCT	800	IGF1R	Ganitumab	M1	1st	Gem	7.0 *vs.* 7.1 *vs.* 7.2 mo OS	Well tolerated, no improvement of survival	Gem + 12 mg/kg, +20mg/kg *vs.* +placebo
Picozzi (2015)(165)	Ib RCT	58	MUC5ac	^{90}Yttrium-clivatuzumab tetraxetan	M1	3rd+	+/-Gem	7.9 *vs.* 3.4 mo* (p=0.004)	* for multiple cycles +Gem OS 2.7 *vs.* 2.6 mo in the whole cohorts	+/- gemcitabine Ab with isotope
Ko (2016)(88)	II	46	EGFR MEK1/2	Erlotinib Selumetinib	LAPC, M1	2nd	no	7.3 mo	No objective responses. In 38% SD in 6w+	59% with additional chemotherapy after study's discontinuation
Coveler (2016)(166)	I	35/50	SLC-44A4	ASG-5ME	M1	2nd+	no	5 mo	Well tolerated, limited tumor activity – 1PR	PC + gastric cancer Ab-drug conjugate against cell-surface target on most PC. & gastric cancers
Beg (2016)(167)	I	4/19	MUC5AC	NEO-102	LAPC, M1	2nd+	no	nr	Well tolerated, no objective responses	PC and colon cancer
Pishvaian (2016)(163)	I	6/39	CEA & CD3 epsilon TCR subunit	MEDI-565	nr	2nd+	no	nr	No objective responses. 28% of all cancer SD at best	GI tumors: Bispecific Ab Pretreated with dexamethasone
Chung (2017)(98)	II RCT	137	MEK PI3K/AKT	Selumetinib MK-2206	M1	2nd	no	3.9 *vs.* 6.7 mo	Shorter survival with immunotherapy	*vs.* oxaliplatin and fluorouracil (FOLFOX)
Benson (2017)(168)	II RCT	240	LOXL2 enzyme	Simtuzumab	M1	1st	Gem	7.6 mo *vs.* 5.9 mo *vs.* 5.7 mo OS	Well tolerated, but no improvement of clinical outcome	3 arns: Gem+Ab 700 mg *vs.* Gem-Ab 200 mg *vs.* Gem+placebo
Almhanna (2017)(169)	II	43	Guanylyl cyclase	MLN0264	LAPC, M1	2nd+	no	5.4 mo	Managable safety but low efficacy , response rate 3%	Ab-drug conjugate
Fountzilas (2017)(89)	II	18	EGFR	Erlotinib	LAPC, M1	1st, 2nd	no	3 mo	Terminated early due to futility	
Cardin (2018)(170)	I	19	Src EGFR	Dasatinib Erlotinib	LAPC, M1	1st	Gem	8 mo	No objective responses. 9 pts had SD	1-y survival 32%
Abdel-Wahab (2018)(90)	I/II RCT	45	IGF-1R EGFR	MK-0646 Erlotinib	M1	1st	Gem	10.4 (A) *vs.* 5.7 mo (C)	Best survival in MK arm, no additional benefit of Erlotinib. Low toxicity	3 arms – A: Gem + MK,B: Gem+MK+E or C: Gem+E
Maurel (2018)(96)	II	25	EGFR	Erlotinib	resected	NAT	Gem+RT	23.8 mo	Better OS for R0 *vs.* R1 resection or not resected: 65.5 mo *vs.*. 15.5 mo, P=0.01	
Dittrich (2019)(171)	Ib	30	EGFR VEGF	Erlotinib Bevacisumab	LAPC, M1	1st in M1	Cap	2.5 mo PFS	Good safety, but limited efficacy.	2 PR, 8/28 SD at 6 mo
Halfdanarson (2019)(92)	II RCT	92	EGFR	Panitumumab, Erlotinib	M1	1st	Gem	4.2 *vs.* 8.3 mo OS	Longer OS with dual inhibition, but increased toxicity	Gem +E *vs.* Gem+E+P
Mettu (2019)(93)	I	21	Src, EGFR	Dasatinib, Cetuximab	LAPC, M1	2nd+	Gem	5.8 mo	Limited clinical effect, but toxicity with both	Solid tumors Gem + Das or Gem + Das/Cet
Davis (2020)(102)	Ib	31	Wnt pathway	Vantictumab	M1	1st	GnP	10 mo	42% PR and 35.5%SD	Terminated due to pathologic-fracture related safety, Max tolerated dose not reached
Hu (2019)(100)	II RCT	177	Notch2/3R	Tarextumab	M1	1st	GnP	6.4 *vs.* 7.9 mo	No diff in OS, even somewhat better in the placebo (p=0.9)	
Wei (2019)(95)	II	114	EGFR	Erlotinib	Resected, head	NAT+ Adj	Gem	21.3 mo 25.4 mo for resected	Feasible	83/114 resected. 52% 2-year survival for resected
Lin (2019)(172)	I/II		CA125 Protease inhib.	Oregovomab Nelfinavir	LAPC	NAT	SBRT + Gem/ leucovorin/ fluoruracil	13 mo	No difference in OS/TTP Compared to a historical group with same Tx	Nelfinavir as radiosensitizer. 4/11 resected
Alewine (2020)(173)	I/II	20	mesothelin	LMB-100 (immunotoxin) + modified Pseudomonas exotoxin A	Advanced, recurrent	2nd +	nPac	nr	1PR, 7 >50% decrease of CA19-9. Not well tolerated	Ab+exotoxin Higher mesothelin expression in pts with tumor marker responses
Bendell (2020)(101)	I	36	MMP9	Andecaliximab	LAPC, M1	1st (in M1)	GnP + Ab	7.8 mo PFS	Well tolerated; PR in 44% (RECIST)	1st line in the metastatic setting
Sinn (2020)(94)	IIb RCT	122	VEGFR, PDGFR, RAF, etc	Sorafenib	Resected R1	1st	Gem	17.6 mo *vs.* 17.5 mo	No diff in RFS no OS	Gem + Ab's *vs.* Gem +placebo
Assenat (2021)(174)	II	63	HER2, EGFR	Trastusumab + Erlotinib	M1	1st	Gem + Ab	OS 7.9 mo	No control group	PFS better when grade >=2 cutaneous toxicity; HER2 and EGFR expression corr with survival on multivariate analysis
Tempero (2021)(99)	III RCT	424	BTK	Ibrutinib	M1	1st	GnP+Ab *vs.* GnP + placebo	9.7 mo *vs.* 10.8 mo	No diff in OS	More side effects and receiving lower dose chemo with Ab
Lim (2021)(91)	II RCT	65	EGFR	Erlotinib	LAPC, M1	1st	GemOx +E versus Gem +E	3.9 mo *vs.* 1.4 mo PFS, not OS (trend)	Better PFS with oxaliplatin,	Ab not tested - Erlotinib in both chemo arms, so unknown benefit

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