**Table S1: Overview of selected studies discussed in the text**
**If not otherwise specified, trials involve patients with locally advanced or metastatic PC**

| Drug/Target | Clinical trial number/name | Phase | Drug |
|---|---|---|---|
| **EGFR** | | | |
| erlotinib | NCT00026338[7] | 3 | Gemcitabine+erlotinib vs. gemcitabine |
| erlotinib (approved) | NCT00440167[8] | 3 | gemcitabine+erlotinib and capecitabine vs capecitabine+erlortinib and gemcitabine |
| cetuximab | NCT00075686[9] | 3 | gemcitabine+cetuximab vs. gemcitabine |
| erlotinib | Conko-005[10] | 3 | gemcitabine+erlotinib vs. gemcitabine (adjuvant) |
| | | | |
| **NTRK inhibitors (approved)** | | | |
| larotrectinib[11] | NCT02122913 | 1 | Larotrectinib in tumors with NTRK fusion |
| | NCT02576431 | 2 | Larotrectinib in tumors with NTRK fusion |
| | NCT02637687 | 1/2 | Larotrectinib in children |
| Entrectinib[12] | NCT02097810 | 1/2a | Entrectinib in tumors with NTRK fusion |
| | NCT02568267 | 2 | Entrectinib in tumors with NTRK fusion |
| | | | |
| **PARP inhibitors** | | | |
| Olaparib[13,14], **approved** | NCT01078662 | 2 | Olaparib in all typs of advanced cancer with a germline BRCA1/2 mutation |
| | NCT02184195 | 3 | Olaparib as maintance therapy for BRCA-mutated pancreatic cancer |
| Veliparib[15-17] | NCT01908478) | 1 | Veliparib plus gemcitabine and radiotherapy in locally advanced disease |
| | NCT01489865 | 1/2 | Veliparib+FOLFOX in metastatic disease |
| | NCT01585805 | 2 | Veliparib+ gemcitabine+cisplatin vs. gemcitabine+cisplatin with advanced pancreatic carcinoma |
| **K-Ras vaccination[18,19]** | | | |
| | (not available) | | Adjuvant vaccination |
| | NCT03592888 | 1 | Dentritic cell vaccine |

| | | | |
|---|---|---|---|
| ***Fibrosis*** | | | |
| **Hedgehog inhibitors** | | | |
| vismogedib[20] | NCT01064622 | 1b/2 | Vismogedib+gemcitabine vs. gemcitabine |
| saridegib[21] | NCT01383538 | 1 | FOLIRINOX+sarigedib |
| vismogedib[22] | NCT01088815. | 2 | vismogedib +gemcitabine/ nab-paclitaxel |
| **Hyoluronidase (Pegvorhyaluronidase Alfa)** | NCT02715804 | 3 | Pegvorhyaluronidase Alfa (PEGPH20)+gemcitabine/nab-paclitaxel vs. gemcitabine/nab-paclitaxel |
| **TGF-beta (galunisertib)[6]** | NCT01373164 | 1b/2 | Gemcitabine+galunisertib vs. gemcitabine |
| **Vitamin A receptor** | NCT03307148 | 2 | ATRA+gemcitabinenab-paclitaxel |
| **VEGF** | | | |
| Axitinib[23] | NCT00471146. | 3 | Gemcitabine+axitinib vs. gemcitabine |
| Bevacizumab[24,25] | NCT00088894 | 3 | Gemcitabine+bevacizumab vs. gemcitabine |
| | NCT00365144 | 3 | Gemcitabine+erlotinib+bevacizumab vs. Gemcitabine+erlotinib |
| | | | |
| **PDL1/PD1** | | | |
| Pembrolizumab,[26] **approved** | NCT02628067 | 2 | Pembrolizumab in dMMR/MSI-high tumors |
| Pembrolizumab (in combination)[27,28] | NCT02826486 | 2a | Pembrolizumab+ motixaforatide with chemotherapy |
| | NCT02620423<br>NCT03723915 | 1b<br>2 | Pembolizumab+pelareorep |
| | NCT03634332 | 2 | Pembrolizumab+PEGPH20 |
| Spartalizumab | NCT04191421 | 1b/2 | Spartalizumab+silutixmab |
| | NCT04581343 | 1 | Spartalizumab+gemcitabine/nab-paclitaxel+canakinumab |
| Durvalumab[29] | NCT02558894 | 2 | Durvalumab+tremilimumab vs durvalumab |
| **CLTA-4** | | | |
| Ipilimumab[30-34] | NCT04787991 | 2 | Ipilimumab monotherapy |
| | NCT00836407 | 1 | Ipilimumab+GVAX |
| | NCT02004262 | 2 | GVAX+CRS-207 |
| | NCT01473940 | 1 | Ipilimumab+gemcitabine |
| | NCT01896869 | 2 | Ipilimumab+ GVAX vs FOLFIRINOX as maintenance therapy |

| | | | |
|---|---|---|---|
| Nivolumab[35] | NCT02243371 | 2 | Nivolumab+GVAX+CRS-207 |
| CD40[36] | NCT00711191 | 1 | Gemcitabine+CD40 monoclonal antibody CP-970-893 |
| IL-10[37] | NCT02923921 | 3 | Pegilodecakin+FOLOFX vs FOLOFX |


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Table S2: Aberrant expression of micro- RNA inculding down and upregulation

| miRNA- | healthy vs pancreatic cancer | PanIn lesions |
|---|---|---|
| 21 | up | |
| 221 | up | |
| 424-5p | up | |
| 27a | up | |
| 4295 | up | |
| 205 | up | |
| 200 | up | |
| 210 | up | |
| 192 | up | |
| 18a | up | |
| 124 | down | |
| 203 | down | |
| 150 | down | |
| 218 | down | |
| 22 | | aberrant |
| 642 | | aberrant |
| 10 | | aberrant |
| 752 | | aberrant |
| 12 | | aberrant |
| 8885-5p | | aberrant |
| 196b | | aberrant |
| 155 | | aberrant |
| 210 | | aberrant |
| 1290 | aberrant | |
| | | |
| **miRNA- & Ca 19.9** | | |
| | | |
| 16 | aberrant | |
| 196 | aberrant | |
| 27a-3p | aberrant | |
| | | |
| | | |
| **miRNA-** | **Expression** | **Survival** |
| 21 | up | worse |
| 10b | up | worse |
| 34a | down | worse |
| 320c | up | better |
| 200b | down | worse |
| 200c | down | worse |
| let 7b | down | worse |
| let 7c | down | worse |
| let 7d | down | worse |

| | | |
|---|---|---|
| let 7e | down | worse |
| 33a | down | worse |
| 15b | down | worse |
| 17-5p | up | worse |
| 155 | up | worse |
| 181c | up | worse |
| 21 | up | worse |
| 203 | up | worse |
| 221 | up | worse |
| 320 | up | worse |
| 33a | down | better |
| 138-5p | down | better |
| 509-5p | down | better |
| 1207 | down | better |
| 1243 | down | better |
| 7 | down | worse |
| 100 | down | worse |
| 124 | down | worse |
| 210 | down | worse |
| 200c | down | worse |
| 205 | down | worse |
| 220b | down | worse |
| 374b-5p | down | worse |
| 497 | down | worse |
| 101-3p | down | better |
| 15 | down | better |
| 203 | down | better |
| 205-5p | down | better |
| 494 | down | better |
| 506 | down | better |
| 3656 | down | better |