

Therapy focus - pancreatic cancer developers press on, despite failures



[Jacob Plieth](#)

The word failure having become synonymous with pancreatic cancer drug development, it will be seen as ironic that the most important advance of recent years concerned the old chemotherapy regimen Folfirinox. That success, in the adjuvant setting, has already derailed one biopharma competitor - Targovax.

This week saw another fall by the wayside as Merrimack canned development of istiratumab after this bombed in a first-line study. Given all the disappointments it might come as a surprise that the industry's mid-stage pancreatic cancer pipeline contains nearly 100 projects, including eight in phase III, with several readouts expected soon (see tables below).

Among the most keenly awaited readouts will be those testing the entry of immuno-oncology into this field, which is one in which anti-PD-(L)1 agents have yet to make their mark. Mid-stage studies of combinations comprising Merck & Co's Keytruda or Bristol-Myers Squibb's Opdivo in the second-line setting could yield data by the end of this year, for instance.

Also, Astrazeneca/Merck & Co's Parp inhibitor, Lynparza, has a phase III readout in the maintenance setting after first-line chemo in germline BRCA-mutated disease. Lynparza will be trying to repeat yesterday's success in the Solo-1 trial of first-line maintenance in ovarian cancer - clearly a less tough disease to treat.

Shifting standards

However, all players will be keeping an eye on Folfirinox. At this year's Asco meeting Folfirinox was declared the likely new standard of care in adjuvant pancreatic cancer treatment after yielding median overall survival of four and a half years - 20 months longer than the current standard, Gemzar.

This [claimed the scalp of Targovax's vaccine TG01](#), as the company admitted that it meant that its study was using the wrong comparator, and that it could not afford to run the five-year clinical trial that would now be needed.

Folfirinox is already an option in first-line disease, and as yet there is no suggestion that it might outperform the entrenched front-line leaders, Gemzar and Celgene's Abraxane. (Roche's Tarceva is also approved first-line, but appears to be a less popular choice.)

However, the French Unicancer consortium is running a first-line treatment study called Neopan that pits Gemzar against Folfirinox and reads out in March 2019. Any suggestion that Folfirinox is better than Gemzar would have serious repercussions on any front-line trial that gives comparator patients Gemzar.

And Folfirinox's adjuvant success could already make for soul-searching among companies such as Fibrogen, whose pamrevlumab is being pitted against Gemzar and Abraxane in a neoadjuvant study. Leerink analysts reckon pamrevlumab's future could hinge on the adoption of a new standard and how resectability is assessed; Fibrogen is to reveal its phase III design in August.

Selected upcoming pancreatic cancer trial readouts

Project	Company	Design	Line of therapy	Status	Primary completion	Trial ID
BL-8040 +/- Keytruda	BiolineRx/Merck & Co	Single-arm (Keynote-202)	2nd-line	Phase II	Jun 2018	NCT02826486
CG200745	Crystalgenomics	Combo with Gemzar + Tarceva; single-arm	1st-line	Phase I/II	Jul 2018	NCT02737228
PEGPH20	Halozyne Therapeutics	Combo with Gemzar + Abraxane	1st-line	Phase II	Sep 2018	NCT01839487
Parvovirus H-1	Oryx	Single-arm	2nd-line	Phase I/II	Sep 2018	NCT02653313
NANT Cancer Vaccine	Nantkwest	Combo with various agents	2nd-line	Phase I/II	Oct 2018	NCT03136406
NANT-008	Nantpharma	Combo with chemo + Avastin	1st-line	Phase I/II	Oct 2018	NCT03127124
Opdivo +/- Yervoy	Bristol-Myers Squibb	Combo with radiation	2nd-line	Phase II	Nov 2018	NCT02866383
LOAd703 oncolytic virus	Lokon Pharma	Combo with Gemzar + Abraxane; single-arm	2nd-line	Phase I/II	Nov 2018	NCT02705196
Lynparza	Astrazeneca/Merck & Co	gBRCA mutated	Maintenance after 1st-line chemo	Phase III	Nov 2018	NCT02184195
MK-0646 +/- Gemzar +/- Tarceva	Merck & Co	Versus Gemzar + Tarceva	2nd-line	Phase I/II	Nov 2018	NCT00769483
Pamrevlumab	Fibrogen	Combo with Gemzar + Abraxane	Neoadjuvant	Phase I/II	Dec 2018	NCT02210559
Abemaciclib +/- LY3023414	Lilly	Versus Gemzar or capecitabine	2nd-line	Phase II	Dec 2018	NCT02981342
AM0010	Lilly	Combo with Folfox	2nd-line	Phase III	Jan 2019	NCT02923921
Gemzar	Unicancer consortium	Versus Folfirinox (Neopan study)	1st-line	Phase III	Mar 2019	NCT02539537
Abraxane	Celgene	Combo with Gemzar (Apact study)	Adjuvant	Phase III	Apr 2019	NCT01964430
Glufosfamide	Eleison	Versus 5-FU	2nd-line	Phase III	Jun 2019	NCT01954992

Source: EvaluatePharma & Clinicaltrials.gov.

In first-line treatment it was in addition to Gemzar and Abraxane that [listiratumab failed](#). This was despite

Merrimack specifically recruiting patients with high serum levels of free IGF-1; a personalised approach is being taken by other groups, too, including Halozyme with PEGPH20 in the hotly awaited Halo-301 study.

Perhaps the most publicised phase III pancreatic cancer readout concerns Lilly's AM010, though this is in the second-line setting; it [passed an interim futility analysis in March](#). This was originated by Armo, a young biotech recently bought out by Lilly for \$1.6bn, and carries with it much of the sector's hope for cytokines and related approaches.

Abraxane was developed by Abraxis Bioscience, a company founded by Patrick Soon-Shiong and sold to Celgene in 2010. It is not surprising to see Mr Soon-Shiong's current biotech ventures such as Nantkwest and Nantpharma also active in the pancreatic cancer field.

Meanwhile, the long-awaited readout of glufosfamide, under development by the private company Eleison Pharmaceuticals, seems to have been delayed. The trial had been due to yield data a year ago, but now has a June 2019 completion date, having been expanded to include Chinese hospitals ([Asco-GI - Pancreatic cancer field awaits sparse data, January 24, 2017](#)).

If pancreatic cancer is already an extremely tough cancer to crack then shifting clinical standards could throw a fresh spanner in the works.

Selected industry assets in phase III pancreatic cancer trials

Project	Company	Mechanism of action	Trial ID
AM0010 (pegilodecakin)	Lilly	IL-10 receptor agonist	NCT02923921
Lynparza	Astrazeneca/Merck & Co	Parp inhibitor	NCT02184195
Masican (masitinib)	AB Science	CD117 inhibitor; FGFR3 inhibitor; PDGFR antagonist	20013-002293-41
Glufosfamide	Elesion	Alkylating agent	NCT01954992
Imbruvica	Johnson & Johnson/Abbvie	BTK inhibitor	NCT02436668
Nanoplatin (demiplatin pegaglumet)	Orient Europharma/Nanocarrier	Nanoparticle-bound chemo	NCT02043288
Napabucasin	Sumitomo Dainippon Pharma	NANOG inhibitor; STAT3 inhibitor; Wnt/beta-catenin signalling pathway inhibitor	NCT02993731
PEGPH20 (hyaluronidase)	Halozyme Therapeutics	Hyaluronan regulator	NCT02715804

Source: EvaluatePharma.

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