ESMO IMMUNO-ONCOLOGY

Annual Congress

A Multi-Center Phase 2a Trial to Assess the Safety and Efficacy of BL-8040 (a CXCR4 inhibitor) in Combination with Pembrolizumab and Chemotherapy in Patients with Metastatic Pancreatic Adenocarcinoma (PDAC)

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Presenter Disclosure

- **Founder and stockholder:** Champions Oncology, Inc., Agenus, Pharmacyte
- **Research support from:** BioLineRx, Erytech, BioExcell
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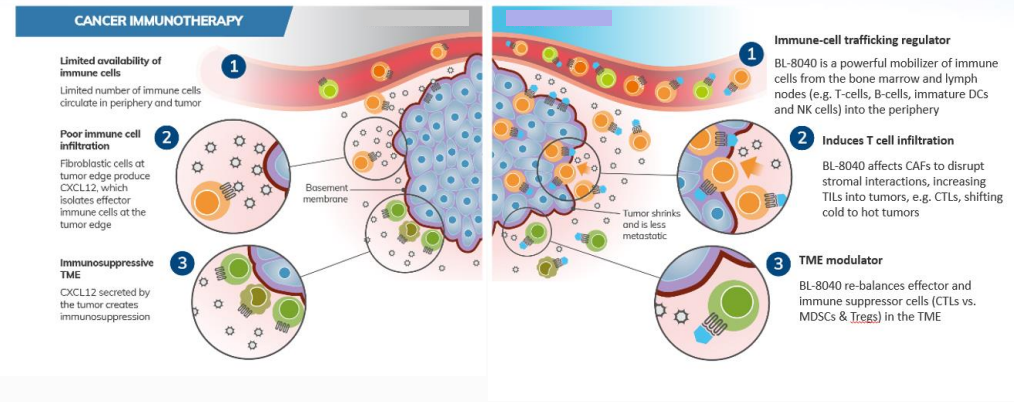
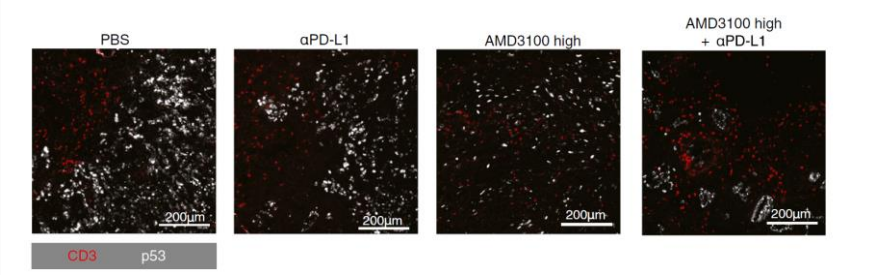
- **Royalties:** Myriad for PALB2 patent.

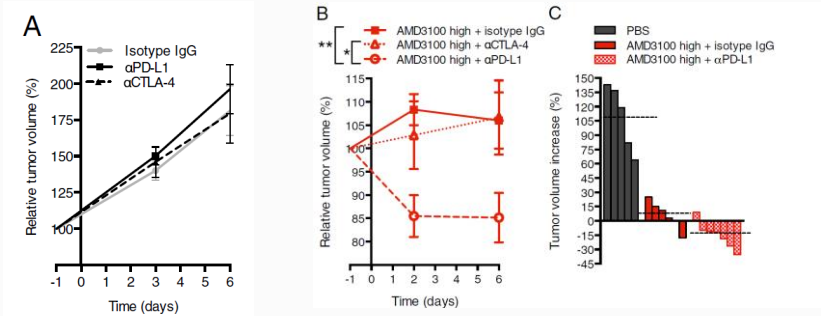
Rationale for the use of BL-8040 (a CXCR4 antagonist) in cancer immunotherapy



CXCR4 and PD-1 Blockade in PDAC Models



α-PD-L1 alone had no effect, whereas CXCR4 antagonist **increased the accumulation of T cells**. The combination of α-PDL-1 with a CXCR4 antagonist amplified this effect and led to an apparent decrease in the frequency of p53 LOH cancer cells

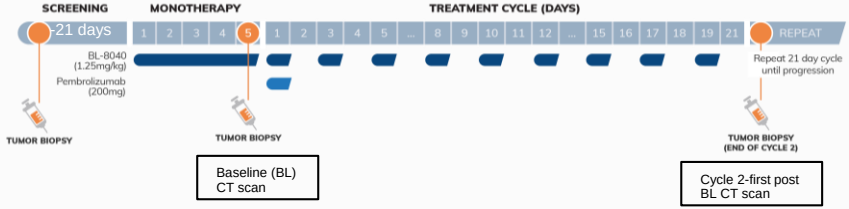


α-PDL-1, α-CTL4 and a CXCR4 antagonist alone had no effect in tumor growth. Only the combination of α-PDL-1 with a CXCR4 antagonist showed decrease of tumour volume

Feig et al 2013

COMBAT- Cohort 1- Dual Combination

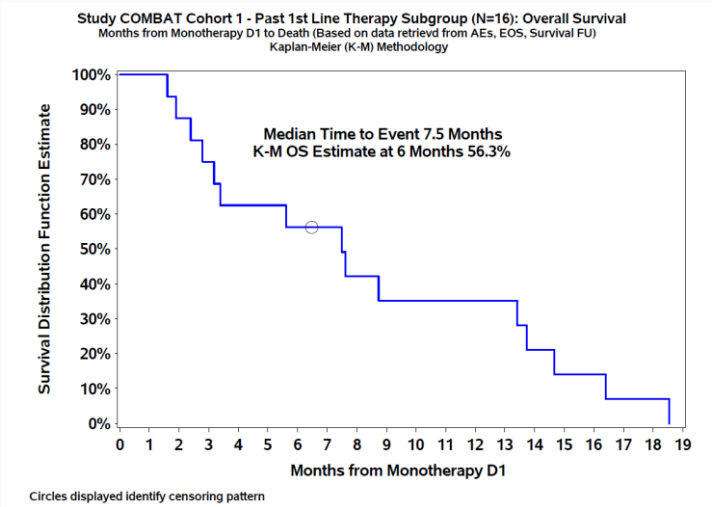
Phase 2a, open-label, multi-center study to assess the safety and efficacy of the high-affinity CXCR4 antagonist BL-8040 in combination with pembrolizumab in patients with metastatic pancreatic cancer; NCT02826486

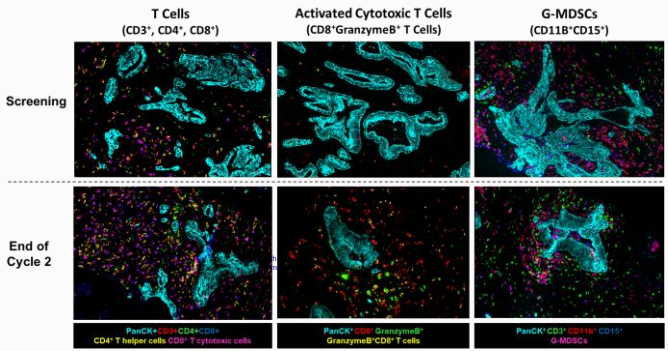


COMBAT- Cohort 1 Dual Combination Results

- 34.5% DCR (PR+SD) for 29 evaluable patients
  - 40% reduction in tumor burden was seen in 1PR
  - 1.5-13% reduction in tumor burden was seen in 6 out of 9 patients with SD
- In all lines of therapy (2L-5L) mOS: 3.3 months
- ***In 2L (N=16) mOS: 7.5 months***

COMBAT- Cohort 1 Dual Combination clinical and biomarker data





- *Increase in activated CD8 T cells*
- *Decrease in MDSCs*
- *Reduction in tumor cell density*

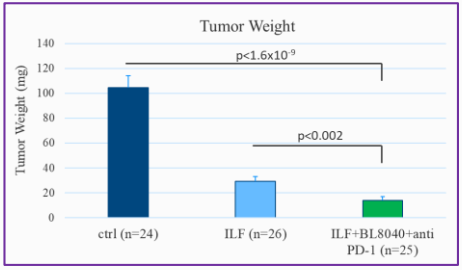
Rationale for Triple Combination (BL-8040+Pembrolizumab+Chemotherapy)

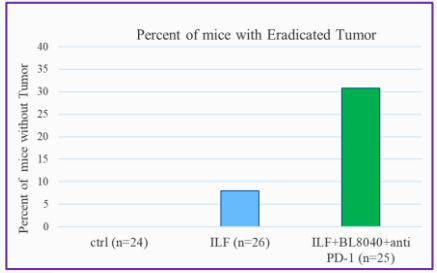
Mechanistic rationale

- Chemo induces tumor death, reducing tumor burden, allowing immunotherapy to kick-in
- Chemo induces immunogenic cell death => activation/expansion of new tumor-reactive T-cell clones
- BL-8040 modulates TME (TILs↑ , MDSC ↓)
- Pembrolizumab maintains/restores T-cell activity in the tumor

Preclinical support

- Synergy of Triple Combo (Chemo+BL-8040+Pembro) in Mouse model





Peleg et al SITC 2019

ILF=irinotecan, 5-FU, Leucovorin

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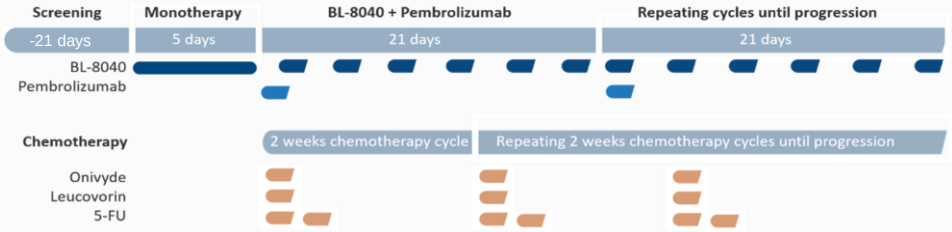
COMBAT/Keynote-202 Cohort 2- Study Design



Main Inclusion/Exclusion criteria

- 18 years old and above
- Metastatic disease at diagnosis (Stage 4)
- Progressed after first-line gemcitabine-based treatment
- No previous surgeries for PDAC
- No prior PD-1 or PDL-1 treatment

COMBAT/Keynote-202 Cohort 2- Study Design- Baseline Demographics

- Total Enrolled N=30: Spain 13, Israel 7, US 10
  - Safety cohort N=30
  - Evaluable patients[1] N=22

Baseline Characteristics	N=30
Gender	Female 43%/Male 57%
Number of prior therapies	1 previous therapy-100%
Median CA 19-9	945.6 (1.2-123112)
Median Age	68 (50-83)
ECOG 0/1	37%/63%

[1] No. of Subjects Treated with the triple combination and have at least one Post Monotherapy D5 (BL) Scan

Data presented based on snapshot as of December 5th 2019

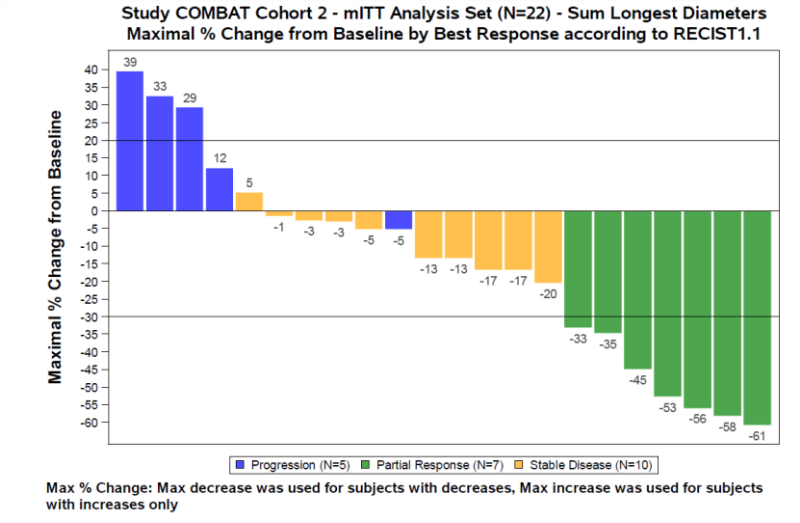
COMBAT/Keynote-202 Cohort 2- Safety

Safety cohort N=30	Any grade, n (%)	Grade 3–4,n (%)
All Adverse events (AEs) Related to any of the study drugs	87.5%	
Adverse events reported in >15% of the patients		
Vomiting	14(47%)	2 (7%)
Diarrhea	13 (43%)	4 (13%)
Asthenia	13 (43%)	3 (10%)
Injection site pain	12 (40%)	1 (3%)
Nausea	12 (40%)	--
Anemia	8 (27%)	1 (3%)
Pruritus	8 (27%)	1 (3%)
Generalized pruritus	7 (23%)	--
Skin Hyperpigmentation	7 (23%)	--
Rash	5 (17%)	--
Decrease Appetite	5 (17%)	2 (7%)

- Combination safety profile is generally consistent with the individual safety profile of each component
- AE and SAE profiles are as expected with chemotherapy-based treatment regimens
- Two subjects early discontinued from study due to Adverse Events

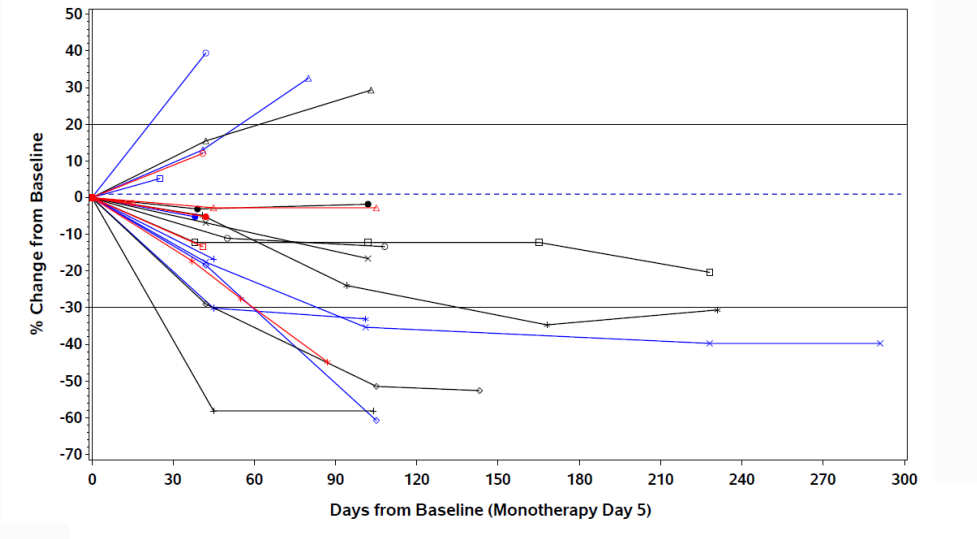
Data presented based on snapshot as of December 5th 2019

COMBAT/Keynote-202 Cohort 2- Change from Day 5 Monotherapy CT scan (BL) in Target lesions (N=22)



	N	%
Evaluable patients	**22**	**100%**
ORR	**7**	**32%**
DCR (PR + SD)	**17**	**77%**
PR	**7**	**32%**
SD	**10**	**45%**

COMBAT/Keynote-202 Cohort 2- Change from Day 5 Monotherapy CT scan (BL) in Target lesions (N=22)



Data shown for subjects treated with the triple combination and have at least one Post Monotherapy D5 (BL) Scan

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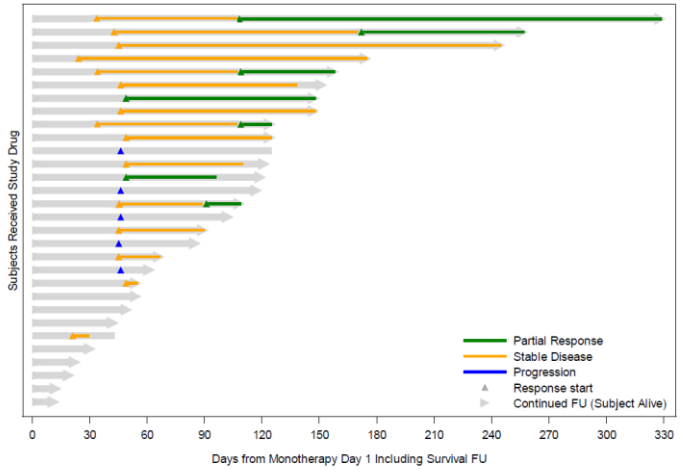
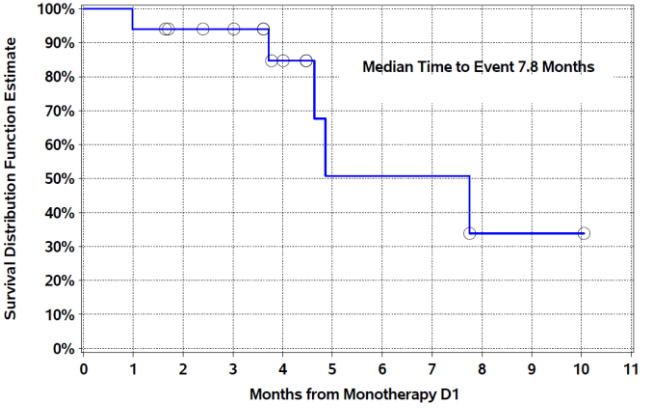
COMBAT/Keynote-202 Cohort 2

Best Response by RECIST & Study Status Over Time. All Patient (N=30)



Subjects with no response category are Non-Evaluable Subjects

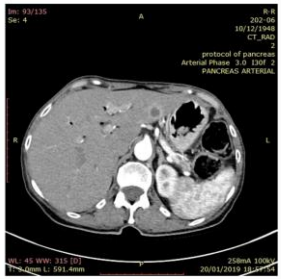
Duration of Clinical Benefit for Subjects with PR (N=7) and SD (N=10)
Months from D1 monotherapy to Disease Progression/Death



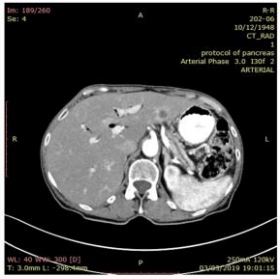
Circles displayed identify censoring pattern

Data presented based on snapshot as of December 5th 2019

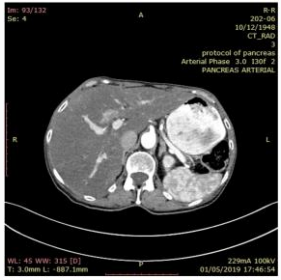
COMBAT/Keynote-202 Cohort 2- Response and CA19-9



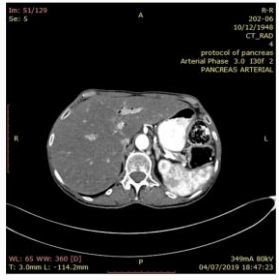
D5 monotherapy- BL



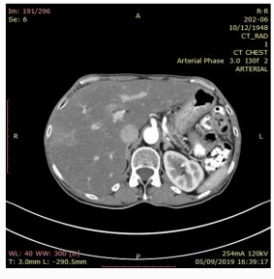
End of Cycle 3



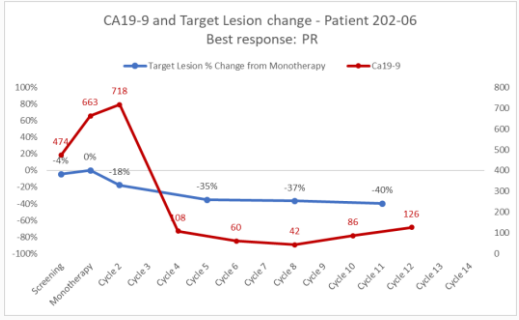
End of Cycle 5



End of Cycle 8



End of Cycle 11



Data presented based on snapshot as of December 5th 2019

Conclusions

- CXCR4 is a chemokine receptor and a validated target overexpressed in many cancer types (including PDAC); overexpression correlates with poor prognosis
- CXCR4 and its ligand, CXCL12, play a critical role in T-cell trafficking, immune cell infiltration, TME modulation, and survival and metastasis of cancer cells
- In this ongoing Phase 2a trial, BL-8040, a CXCR4 antagonist, when combined with Pembrolizumab and Onivyde, 5FU and Leucovorin, demonstrates a tolerable safety profile generally consistent with the profile of each of the components alone
- Preliminary data from the triple-combination cohort in this trial demonstrate promising ORR and durable clinical benefits from the study regimen as second line therapy in patients with advanced pancreatic cancer
- Further studies of the combination of BL-8040, Pembrolizumab and chemotherapy are warranted in pancreatic cancer, as well as other indications historically unresponsive to checkpoint inhibitors and/or chemotherapy

Acknowledgments

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- The clinical study teams who participated in this trial
    - Merck & Co., Inc. (Kenilworth, NJ, USA)
    - BioLineRx (Modiin, Israel)
- All authors contributed to and approved the presentation

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