BerGenBio

Axl inhibitors for aggressive disease

Corporate Presentation

January 2020

Forward Looking statements

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BerGenBio corporate over view

World leaders in understanding AXL biology

AXL tyrosine kinase is a novel drug target that mediates immune evasion, therapy resistance & metastasis

AXL mediates EMT, stabilises M2 macrophages, immune suppressive dendritic cells and blocks T-cell & NK cell activity

AXL inhibitors – potential cornerstone of cancer therapy

Pipeline opportunities in multiple cancers and fibrosis

3 selective AXL inhibitors in clinical development

Bemcentinib (oral once a day pill)
Tilvestamab (mAb), ADCT601* (ADC)

Phase II: Monotherapy and combos with, CPI, targeted & chemo

Biomarker correlation, parallel CDx development

Bemcentinib clinical development focus
AML (monotherapy), **AML** (chemo-combo)
NSCLC (KEYTRUDA combo)

Resourced to deliver milestones

Listed on Oslo Børs: BGBIO

Clinical trial collaborations with Merck and leading academic centres EU & USA

38 staff at two locations:
HQ & R&D in Bergen, Norway;
Clinical Development in Oxford, UK

*AXL antibody out licensed to ADC Therapeutics SA

Management Presenting team

Richard S. Godfrey, *Chief Executive Officer*

- Pharmacist / MBA – joined BerGenBio in 2008 as CEO
- 30 years industry experience, led and managed multiple international drug development and commercialization partnerships
- Formerly Eli Lilly, Reckitt Benckiser, Catalent, DDC.
- Developed and launched several drugs in different classes: Adalat, Noctura, Feldene, Imodium, Pepcid, Zyprexa, Zofran, Subutex

Prof. James Lorens, *Founder and Chief Scientific Officer*

- Professor University of Bergen Medical School
- 30 years biotech research experience, academic biomedical research positions at Stanford University and University of Bergen
- Former Director Oncology R&D, Rigel Inc. (San Francisco, CA)
- The first to recognize that Axl kinase is an essential mediator of cancer development (EMT)

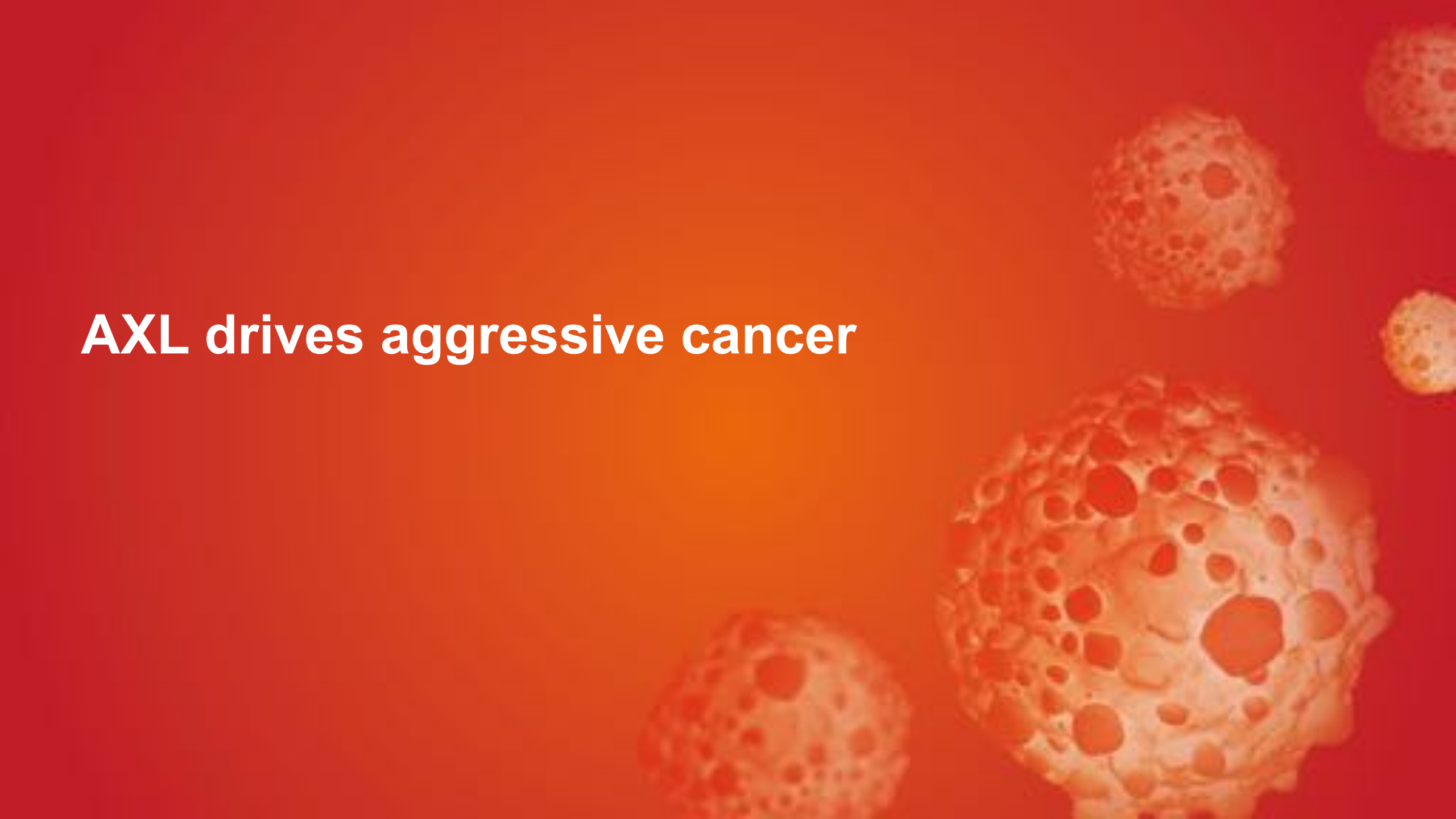
Prof. Hani Gabra MD, PhD, *Chief Medical Officer*

- MD Oncologist – joined BerGenBio in 2019
- Former VP Clinical Development Astra Zeneca UK.
- Professor of Medical Oncology at Imperial College London and Honorary Consultant in Medical Oncology at Imperial College Healthcare NHS Trust
- 20 years clinical / cancer biology research at Imperial College London.

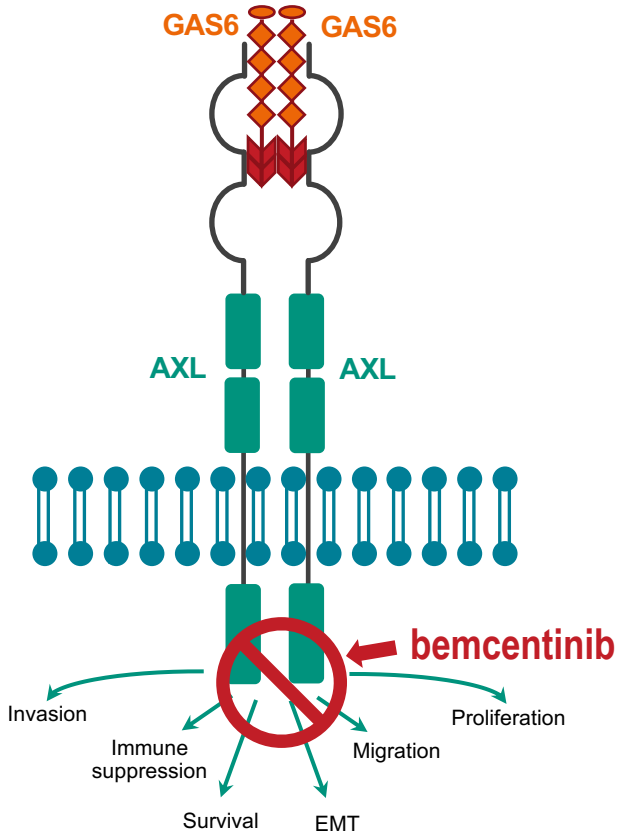
Rune Skeie, *Chief Financial Officer*

- 20 years of financial management, corporate development, corporate governance and advisory experience across multiple industry sectors. – Joined BerGenBio in 2018
- Previously Executive Director at EY and CFO of REMA Franchise Norge AS, the multinational supermarket business.
- Registered Accountant and a State Authorized Public Auditors

AXL drives aggressive cancer



AXL Biology and bemcentinib Mode Of Action



- AXL is a member of the Tyro3, AXL, Mer (TAM) family of receptor tyrosine kinases
- It functions as a homeostatic regulator in adult tissues and organ systems that are subject to continuous challenge and renewal throughout life – immune, nervous, vascular and reproductive
- AXL and its ligand - Growth Arrest Specific Factor (Gas6) - are essential for the efficient phagocytosis of apoptotic cells and membranes in these tissues; and in the immune system, they act as pleiotropic inhibitors of the innate inflammatory response to pathogens
- Abnormally elevated AXL signalling is strongly associated with cancer progression, metastasis, and resistance to targeted therapies.
- Bemcentinib is a first-in-class highly selective, potent, and orally bioavailable inhibitor of AXL

Very low expression under healthy physiological conditions	Elevated AXL signalling strongly associated with cancer progression, metastasis and resistance to targeted therapies	Overexpression correlates with worse prognosis in most cancers

[1]Lemke; Cold Spring Harb Perspect Biol 2013

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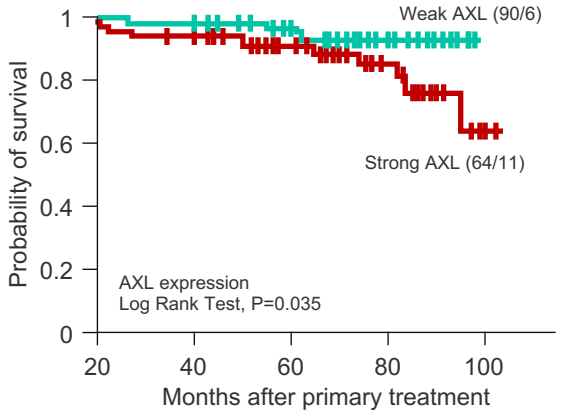
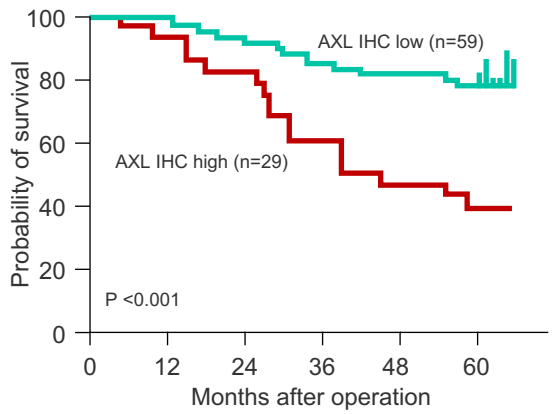
AXL is independent negative prognostic factor in a broad variety of cancers

Strong AXL expression correlates with poor survival rate

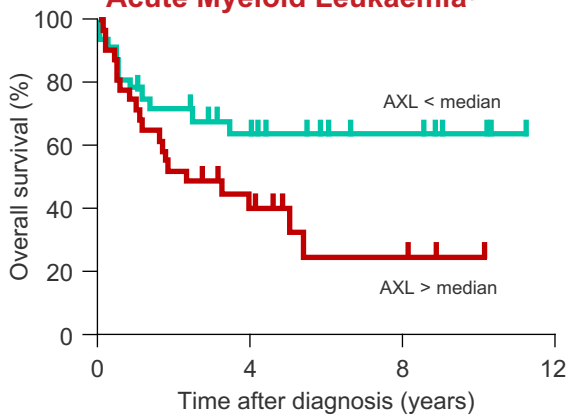
Breast carcinoma[1]



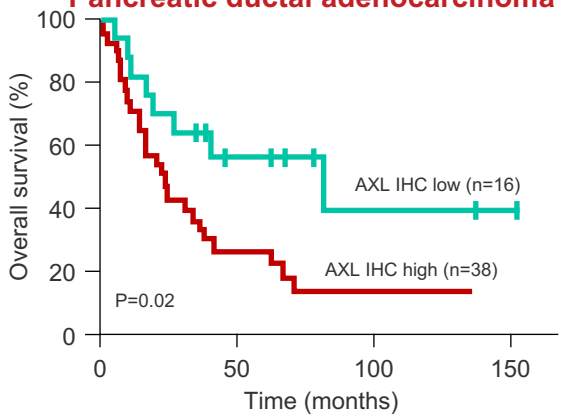
Lung adenocarcinoma (NSCLC)[2]



Acute Myeloid Leukaemia[3]



Pancreatic ductal adenocarcinoma[4]



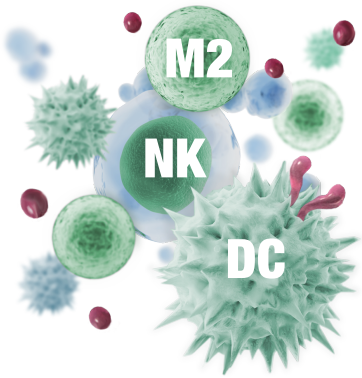
Broad evidence of AXL linked with poor prognosis[5]

Astrocytic brain tumours	Melanoma
Breast cancer	Mesothelioma
Gallbladder cancer	NSCLC
GI	Pancreatic cancer
• Colon cancer	Sarcomas
• Oesophageal cancer	• Ewing Sarcoma
• Gastric cancer	• Kaposis sarcoma
Gynaecological	• Liposarcoma
• Ovarian cancer	• Osteosarcoma
• Uterine cancer	Skin SCC
HCC	Thyroid cancer
HNC	Urological
Haematological	• Bladder cancer
• AML	• Prostate cancer
• CLL	• RCC
• CML	

1 Gjerdrum, 2010; 2 Ishikawa, 2012; 3 Ben-Battala, 2013; 4 Song, 2010, 5 supported by > 100 publications

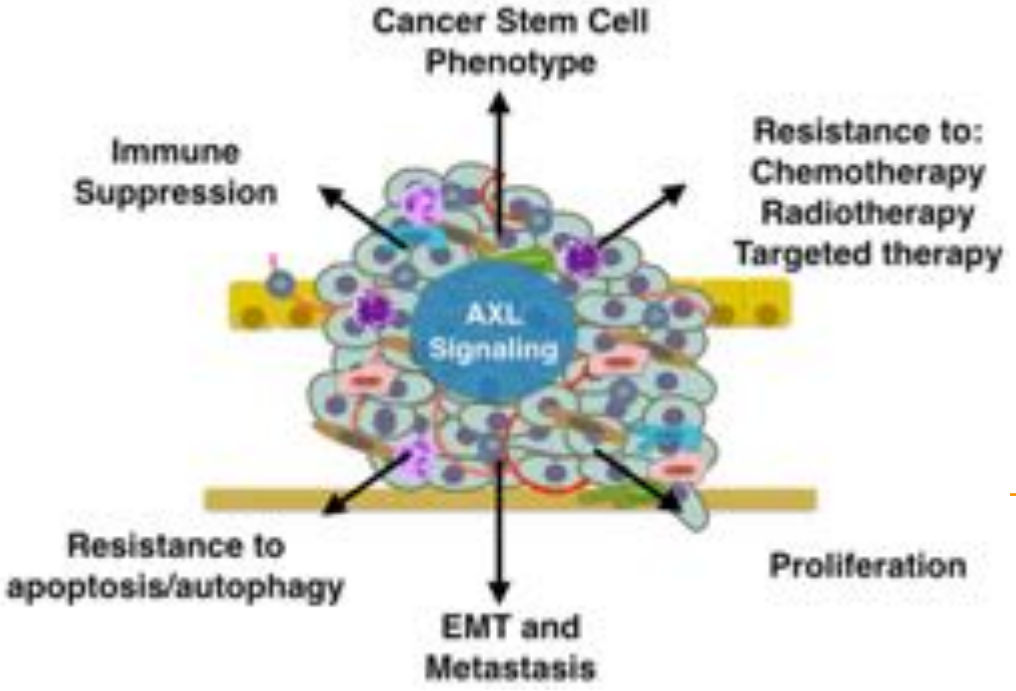
AXL is a key survival mechanism ‘hijacked’ by aggressive cancers and drives drug resistance, immune-suppression & metastasis

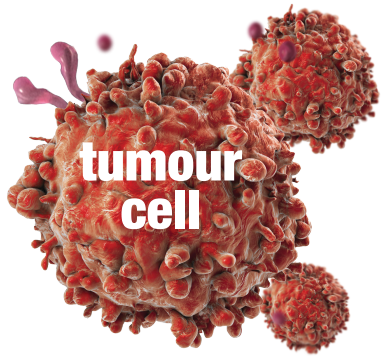
very low expression under healthy physiological conditions → overexpressed in response to hypoxia, inflammation, cellular stress & drug treatment → overexpression correlates with worse prognosis in most cancers



AXL increases on immune cells and suppresses the innate immune response

- M1 to M2 macrophage polarisation
- Decreased antigen presentation by DCs
- Prevent CD8+ T cell mediated cell death
- Activates Treg cells



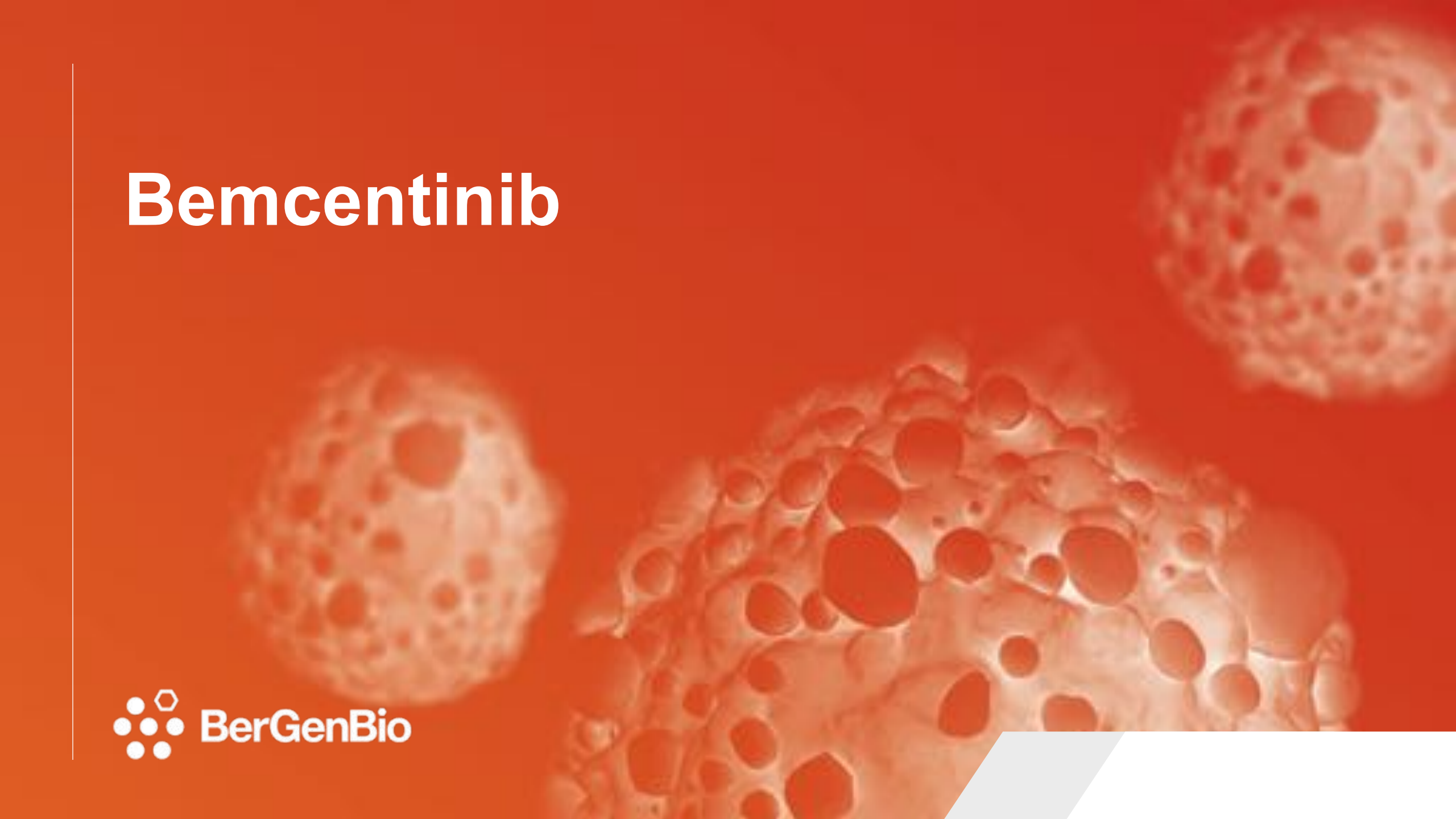


AXL increases on the tumor cell and causes cancer escape and survival

- AXL is a unique type I interferon (IFN) response checkpoint
- Acquired drug resistance
- Immune cell death resistant
- Metastasis

DC- dendritic cells Treg – Regulatory T Cell

Bemcentinib



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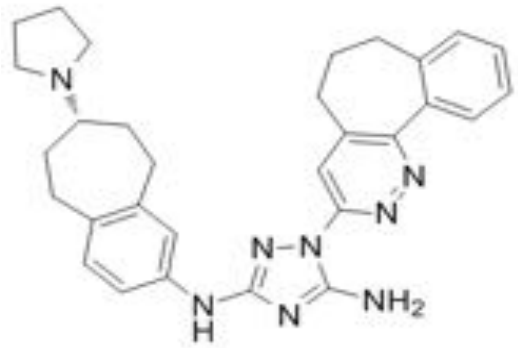
Bemcentinib, a first-in-class, potent, oral, highly selective AXL inhibitor



- ✓ IC_{50} = 14 nM
- ✓ 50-100 fold selective *cf.* TAM kinases

- ✓ CMC scaled for regulatory filing
- ✓ Size 0 100mg HPMC capsules
- ✓ 3 years stability confirmed

- ✓ Uniquely selective for AXL
- ✓ MOA is synergistic with other Immunotherapies enhancing response
- ✓ Favourable safety and tolerability profile supports broad use in lower risk first line as well as advance elderly fragile patients
- ✓ Once daily oral dosing
- ✓ Fast Track Designation by FDA for AML
- ✓ Safety and tolerability profile supports use in combination with chemo, targeted and IO drugs

BerGenBio pipeline - 3 selective AXL inhibitors in clinical development

Multiple attractive opportunities in AML and NSCLC

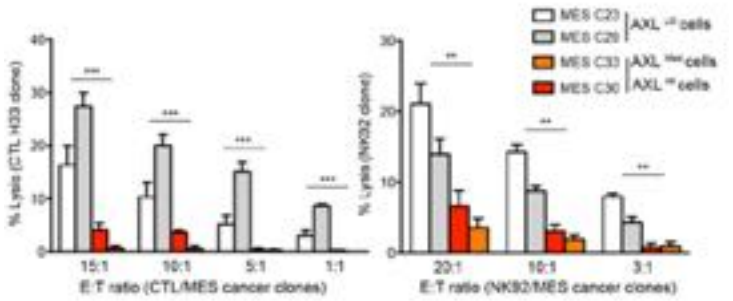
Candidate	Targeted Indication	Discovery	Preclinical	Phase I	Phase II	Phase III.
Bemcentinib	>2L AML	Ph II safety and POC efficacy demonstrated in 39 patient trial				
Bemcentinib (combination with LDAC)	2L AML	Ph Ib Safety demonstrated, efficacy POC expansion study- 28 pts.				
Bemcentinib (combination with Keytruda) MERCK	2L NSCLC. (chemo refractory)	Ph II safety and POC efficacy demonstrated in 50 patient trial, end points met				
	2L NSCLC (CPI refractory)	Ph II POC study on going 29 pts – stage 1 met end point				
	2L NSCLC (CPI+chemo refractory)	Ph II POC study on going 29 pts				
Tilvestamab (BGB149)	TBA	Ph I Healthy volunteer study ongoing				
BGB601 ADC THERAPEUTICS	Various solid tumors	Ph I safety study ongoing				

CPI – checkpoint inhibitor

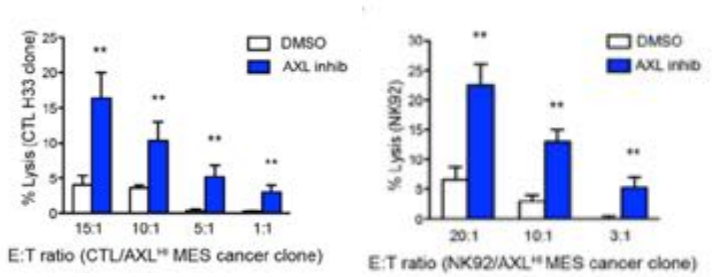
Preclinical data at AACR reinforces bemcentinib's potential to reverse tumour immunosuppression and therapy resistance

Chouaib *et al*

NSCLC cells high in AXL are less susceptible to destruction by T- and NK cells



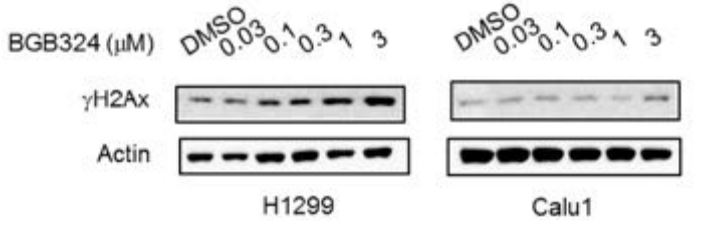
Bemcentinib treatment of the tumour cells with high AXL expression reverses this effect



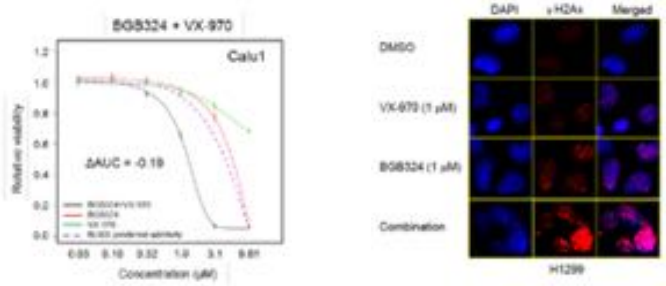
Key pre-clinical data supporting the rationale of combining bemcentinib with IO / bemcentinib's IO MoA

Ramkumar, Byers *et al*

Bemcentinib dose-dependently induces DNA damage in NSCLC cells (γH2Ax is a marker of DNA damage



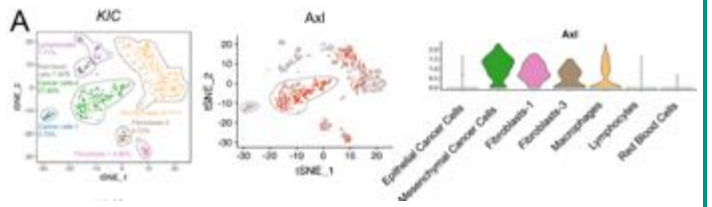
Bemcentinib has synergistic effect when given in combination with DNA damage targeting agents (VX-970)



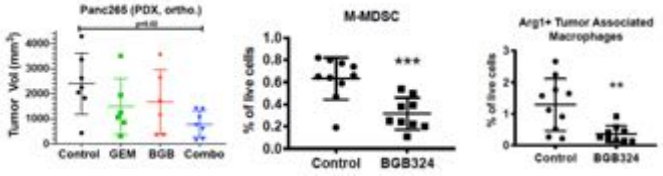
Supports the rationale of combining bemcentinib with chemo and DNA damaging agents

Du, Brekken *et al*

AXL highly expressed in pancreatic tumour models, particularly in cancer cells, fibroblasts & macrophages



Bemcentinib has synergistic effect when given in combination with chemo, reverses immunosuppression



Supports the rationale of combining bemcentinib with chemotherapy & bemcentinib's IO MoA

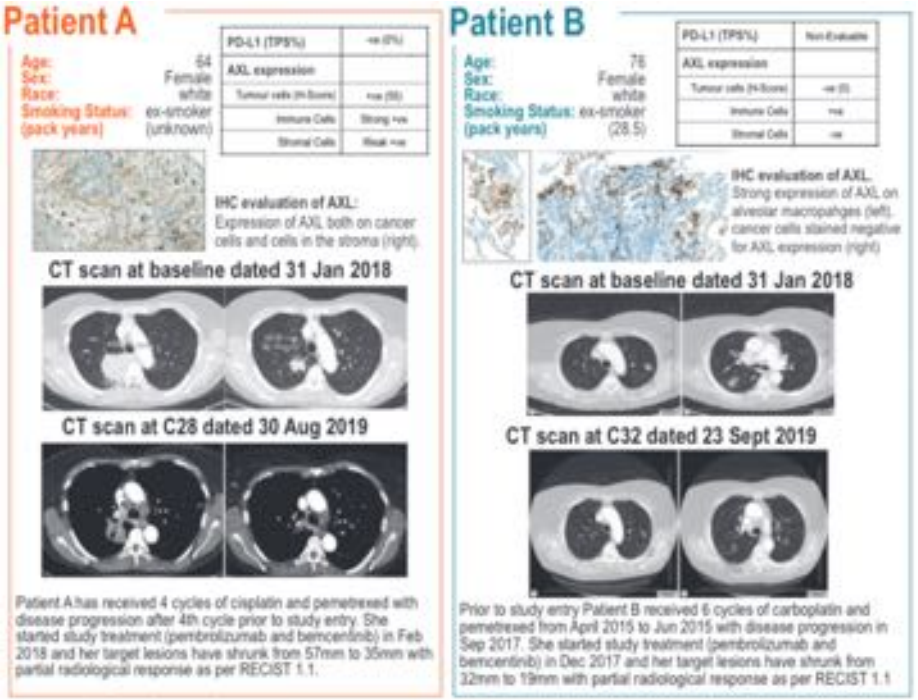
BerGenBio provided drug and in some instances part funding for the work

Potential label expansion with additional phase II studies with bemcentinib

		Clinical Proof-of-concept	Late stage Opportunities
Monotherapy Selected, biomarker directed patients	AML / MDS	Completed	
	Glioblastoma (IIT)	Ongoing	
	Ovarian (EMT signature selected)	Potential	
Chemotherapy Combinations Improve responses in hard to treat settings	AML + LDCT (LDAC)	Complete. -EXPANSION	
	Pancreatic, (IIT)	Ongoing	
	NSCLC (IIT)	Ongoing	
Immunotherapy Combinations Target resistance, enlarge addressable patient population	NSCLC (PD-L1 / AXL all comers)	Cohort A Complete Cohort B ongoing	
	Melanoma, (IIT)	Ongoing	
	Mesothelioma (IIT)	In set-up	
	Bladder ++, CAR-T combos	Under consideration	
Targeted Therapy Combinations Target resistance, enlarge addressable patient population	NSCLC + EGFRi	Completed	
	Melanoma, (IIT)	Ongoing	
	PARPi combos ++	Under consideration	
Earlier Line Opportunities Radiotherapy and maintenance opportunities	Multitude of maintenance opportunities given very favourable safety profile		

Companion Diagnostic (CDx)

- Developed a proprietary duplex IHC method with composite AXL tumor-immune Score (cAXL)
- A proprietary diagnostic algorithm using IHC scoring of AXL on tumor cells and on immune cells to identify solid tumour (NSCLC) patients that will respond / benefit from bemcentinib + CPI



Patient A: RESPONDER
- AXL stained +ve on tumor cells
- 61% tumor shrinkage

Patient B: RESPONDER
- AXL stained -ve on tumor cells
- AXL stained +ve on alveola macrophages
- 59% tumor shrinkage

AXL mediates aggressive cancer traits through EMT and Immune suppression in the tumour microenvironment:

Patient A: AXL +ve staining on lung tumour cells

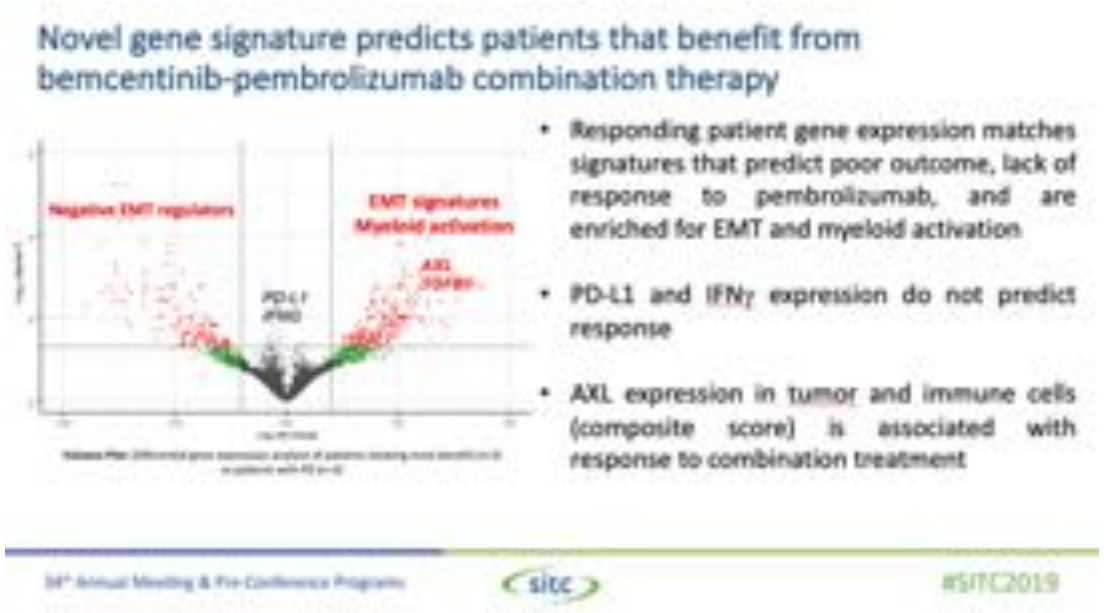
- AXL mediated EMT in tumour cells
- AXL+ve Mesenchymal tumour cells are drug resistant & immune evasive

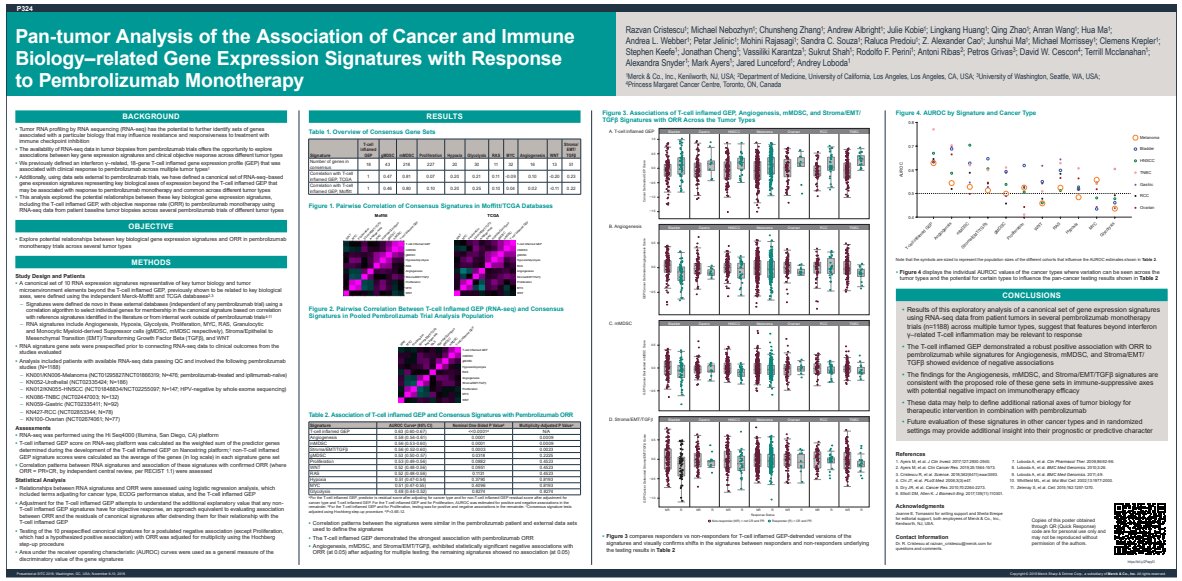
Patient B: AXL +ve staining on lung macrophages

- AXL is required to stabilize M2 macrophages
- M2 microphases are immune suppressive
- Bemcentinib inhibits AXL and macrophages switch to M1
- M1 macrophages are immune promoting

BerGenBio's proprietary novel gene signature predicts patients that benefit from bemcentinib - pembrolizumab combination therapy

SITC 2019: BerGenBio & Merck independently published related gene signatures that predict response or resistance to pembrolizumab





Merck reported a gene signature from patients that did not respond to Keytruda monotherapy in many cancers, this was similar to the BerGenBio gene signature EXCEPT these patients did respond to Keytruda + bemcentinib

AXL inhibitors – emerging competitive landscape

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Ref. BGBC003 / NCT02488408

Bemcentinib clinical development in Acute Myeloid Leukemia (AML) and Myelodysplastic syndromes (MDS)

Objective: to evaluate the safety and efficacy of bemcentinib in AML and MDS

- Bemcentinib monotherapy in patients relapsed AML or MDS
- Bembentinib in combination with low-dose cytarabine (LDAC) in 1L newly diagnosed or relapsed patients with AML
- Bembentinib in combination with LDAC in 2L relapsed patients with AML

Acute Myeloid Leukaemia (AML)

Most common type of acute leukaemia in adults[1]

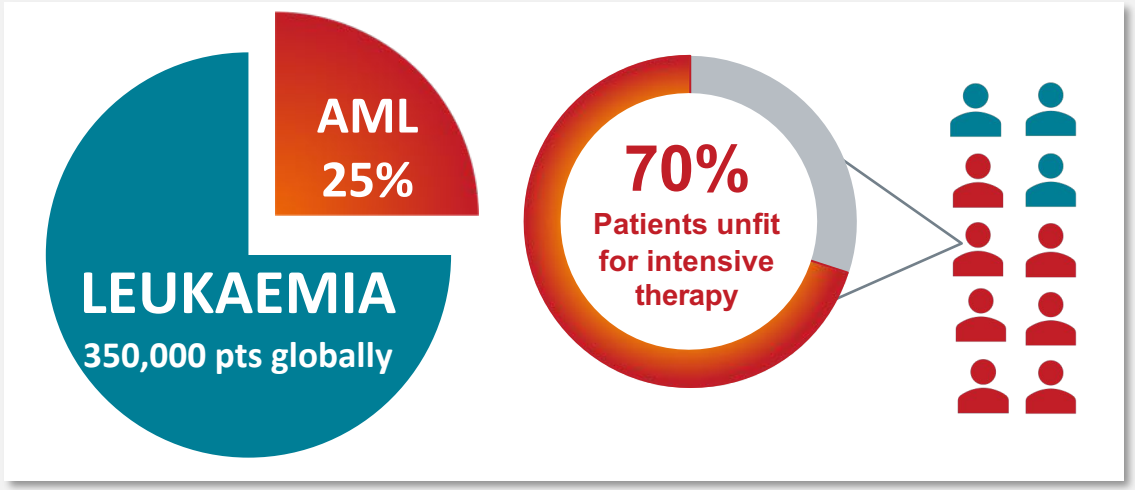
AML is a rare aggressive cancer of the blood and bone marrow characterised by difficult to treat malignancies

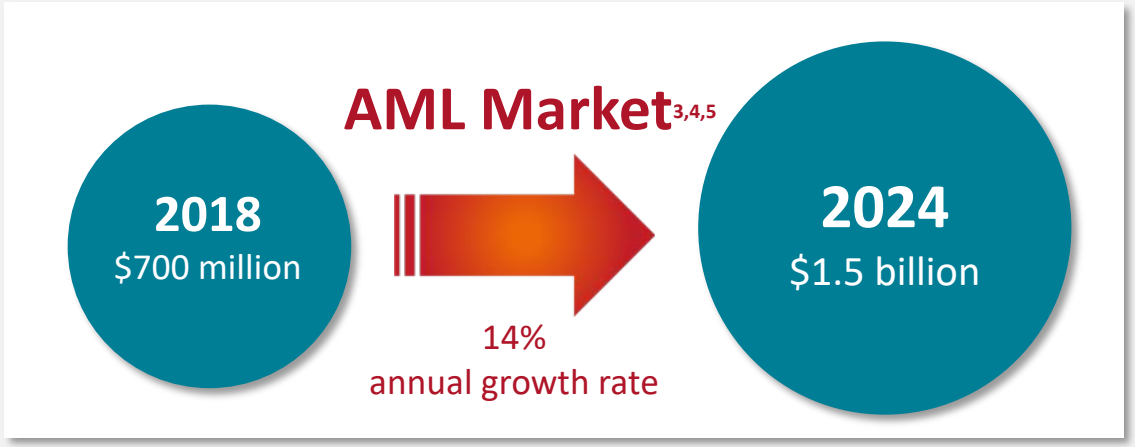
~ 21,000 new cases diagnosed and >11,000 deaths in the US in 2018[2]

AML makes up 32% of all adult leukaemia cases

Occurs in a predominantly elderly, frail patient population; 68% of patients diagnosed with AML were aged >60 years [6]

5 year survival rates of 3-8% in patients over 60 years old [7]





(1) Cancer.gov; (2) SEER; (3) https://www.who.int/selection_medicines/committees/expert/20/applications/AML_APL.pdf?ua=1ble
(4) https://www.cancer.net/cancer-types/leukemia-acute-myeloid-aml/statistics (5) https://www.businesswire.com/news/home/20190319005442/en/ (6) http://asheducationbook.hematologylibrary.org/content/2010/1/62.long, (7) https://www.ncbi.nlm.nih.gov/books/NBK65996/

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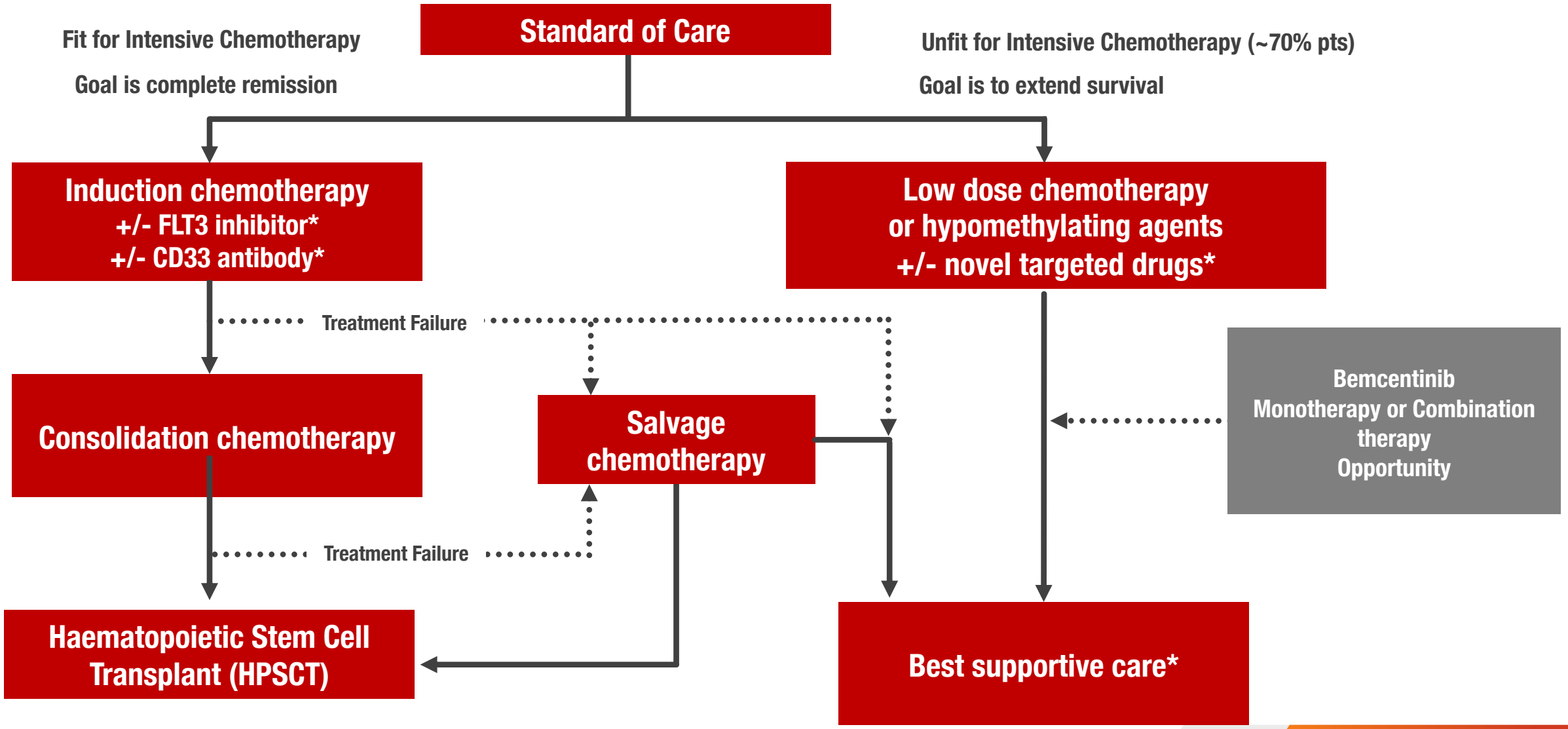
Acute Myeloid Leukaemia: Standard of Care & Bemcentinib Positioning



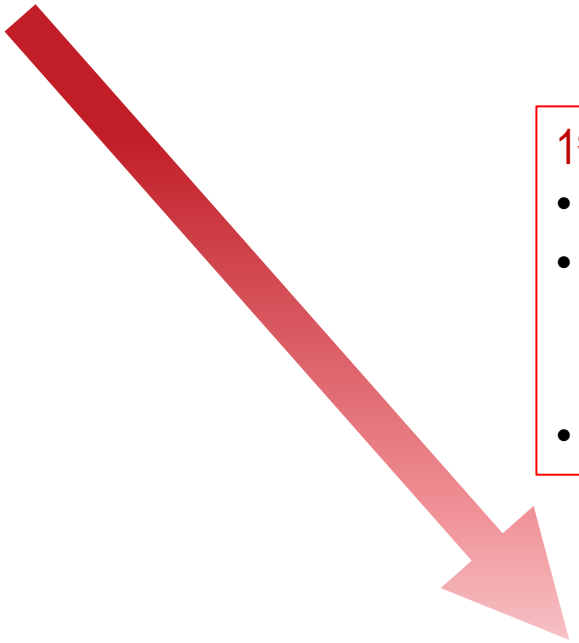
*A small number of patients may be eligible for targeted therapy

Current Approach to AML in Elderly Patients Unfit for Intensive Chemotherapy

Newly Diagnosed AML: Choice of Low Intensity Induction Therapy:

- Hypomethylating agent (HMA) +/- venetoclax (approved in US only)
- LDAC alone or in combination with venetoclax or glasdegib (approved in US only)
- Future direction: AML with mutation of FLT3, IDH1/2

Opportunity for Bemcentinib + LDAC



1st Relapse

- Clinical trial
- No approved therapy, but options may include HMA, LDAC or single agent venetoclax dependent on funding
- Best supportive care (BSC) or palliative care

2nd Relapse

- Clinical trial
- BSC or palliative care

Opportunity for Single Agent Bemcentinib

Bemcentinib clinical development in Acute Myeloid Leukemia, (BGBC003)

Phase 1 n=36

Single agent bemcentinib dose-finding in r/r AML/MDS

Established safety and recommended Phase 2 dose in this population

Recommended Phase 2 dose of bemcentinib in AML or MDS is 400/200 mg as single agent OR in combination. No dose adjustment required.

Phase 2 Expansion Cohorts

- Cohort B1 n=14 Monotherapy AML
- Cohort B2 n=16 Combination with LDAC in newly diagnosed or relapsed AML
- Cohort B5 expansion Combination with LDAC relapsed AML (ongoing)
- Cohort B3 n=14 Combination with decitabine in ND or relapsed AML
- Cohort B4 n=14 Monotherapy MDS

LDAC = Low Dose Cytarabine

Results of the Phase 1 Bemcentinib monotherapy in relapsed/refractory AML

(Loges et al ASH 2018)

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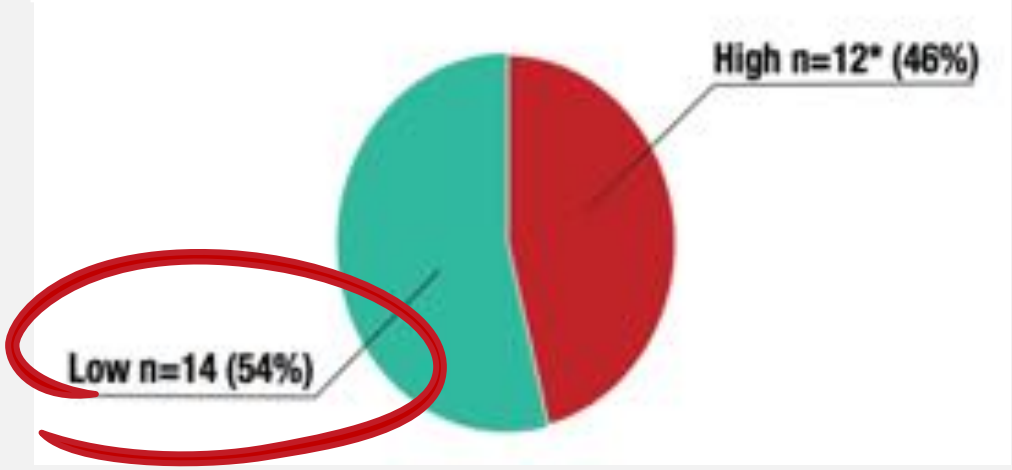
Bemcentinib monotherapy in ≥2L r/r AML patients >75 yrs.

	Overall (n=27)		sAXL low (n=14)		sAXL high (n=11)	
	n	%	n	%	n	%
CR/CRi/CRp	6	22%	6	43%	0	0%
SD	8	30%	3	21%	5	45%
PD*	13	48%	5	36%	6	55%
ORR	**6**	**22%**	**6**	**43%**	**0**	**0%**

- 2 evaluable patients were not evaluable for sAXL status
- Monotherapy responses. One additional response was reported in combination with decitabine for a total of 7 responses in phase I/II.
- 1 CR, 4 CRi, 1 CRp

* PD includes patients who progressed or came off study before having completed 2 cycles of treatment

Biomarker: Soluble AXL (sAXL) at screen:
Inversely correlated with AXL receptor activity



≥2L Relapse patients >75yrs
No approved SoC
Bemcentinib Monotherapy
ASH 2018

AXL +ve patients*
14/27
54%

CR/Cri/CRp
6/14
43%

Stable Disease
3/14
21%

mDOR **3.1mo. (5.5* mo.)**

Safety profile was well tolerated

* including 2 patients with low dose decitabine, one remains in CR after 20 months

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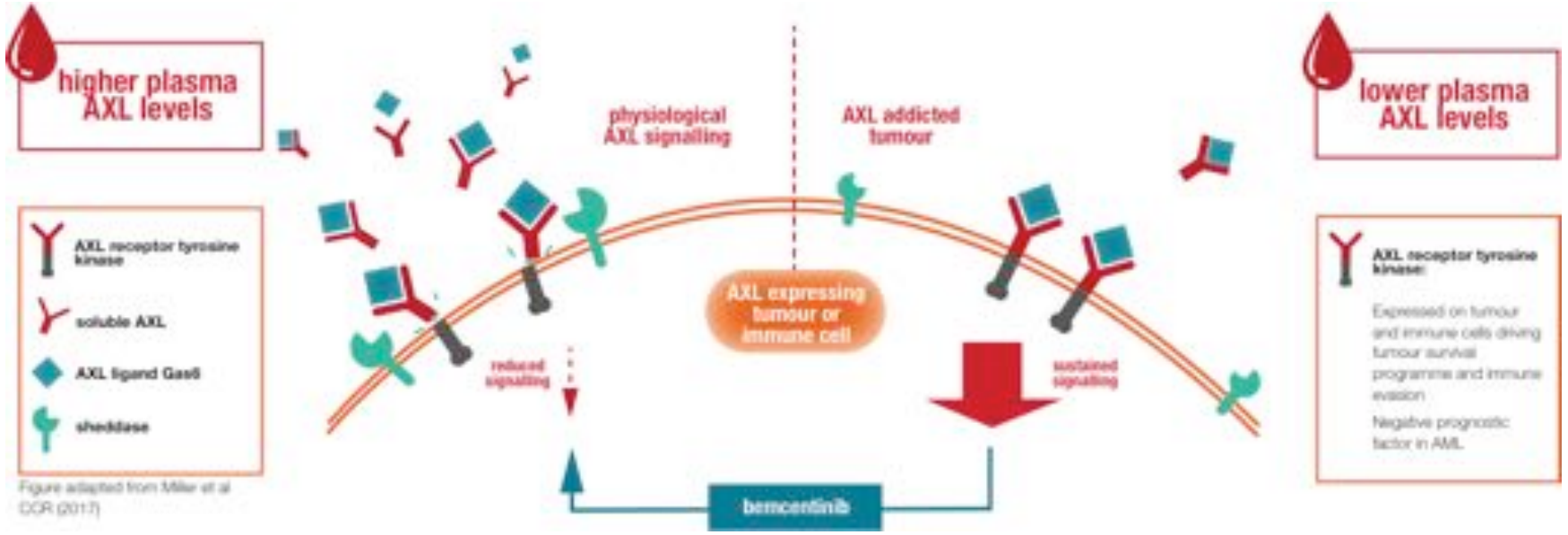
AXL receptor tyrosine kinase is negatively regulated by receptor shedding

plasma sAXL level correlates inversely with AXL signalling

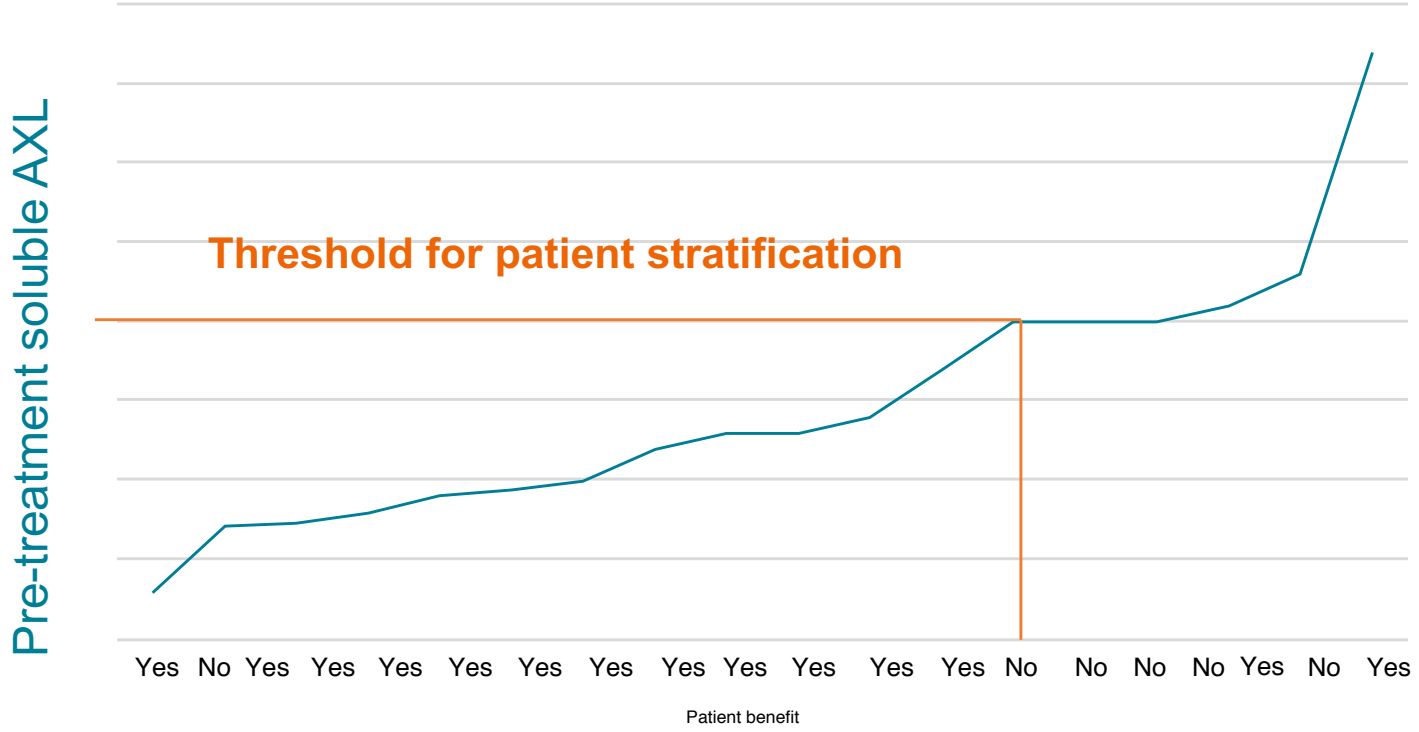
low plasma sAXL is predictive of clinical benefit



sAXL^{low} : low receptor shedding
Activated AXL receptor and signalling > benefit from AXL inhibition with bemcentinib

sAXL^{high}: Increased receptor shedding
Reduced AXL receptor activation and signalling

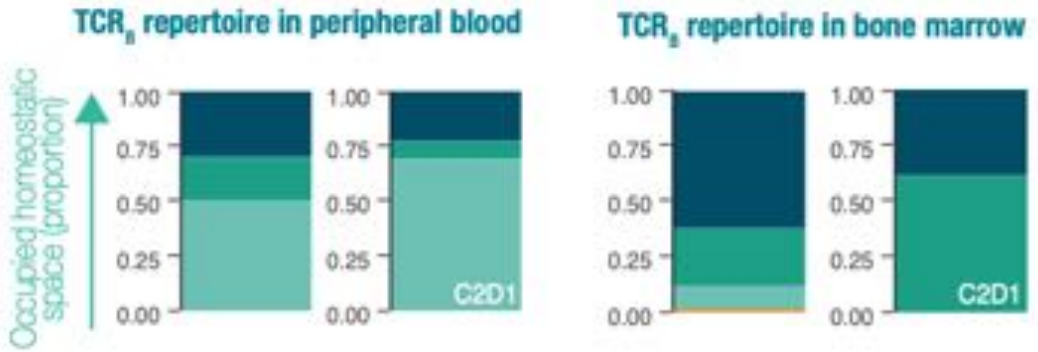
sAXL levels at baseline predict patient benefit to bemcentinib monotherapy (& LDAC combination) in AML



Pre-treatment sAxl levels in plasma samples taken from AML and MDS patients in BGBC003. An example cut-off for patient stratification is presented.

Loges, ASCO 2018

Bemcentinib monotherapy in AML patients led to TCR/BCR diversification: indicative of an immune response



Pt is a 76 yo white female, with poor-risk disease. Relapse after 3 prior lines of low intensity therapy. Stable disease > 3 months on bemcentinib monotherapy.

- Small (1e-05 < X ≤ 1e-04)
- Medium(1e-04 < X ≤ 0.001)
- Large (0.001 < X ≤ 0.01)
- Hyperexpanded (0.01 < X ≤ 1)

Loges ASH 2018

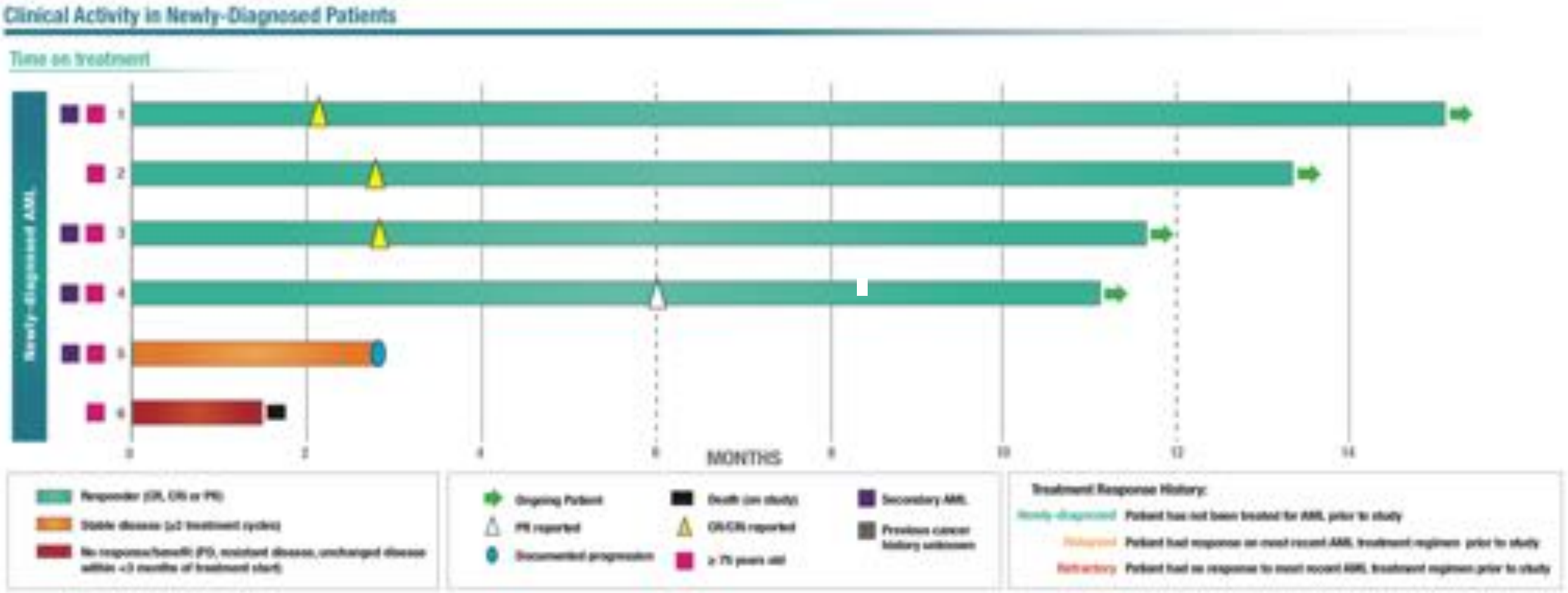
Results of the Phase IIa of LDAC+ Bemcentinib combination in newly diagnosed and relapsed/recurrent AML

(Loges et al ASH 2019)

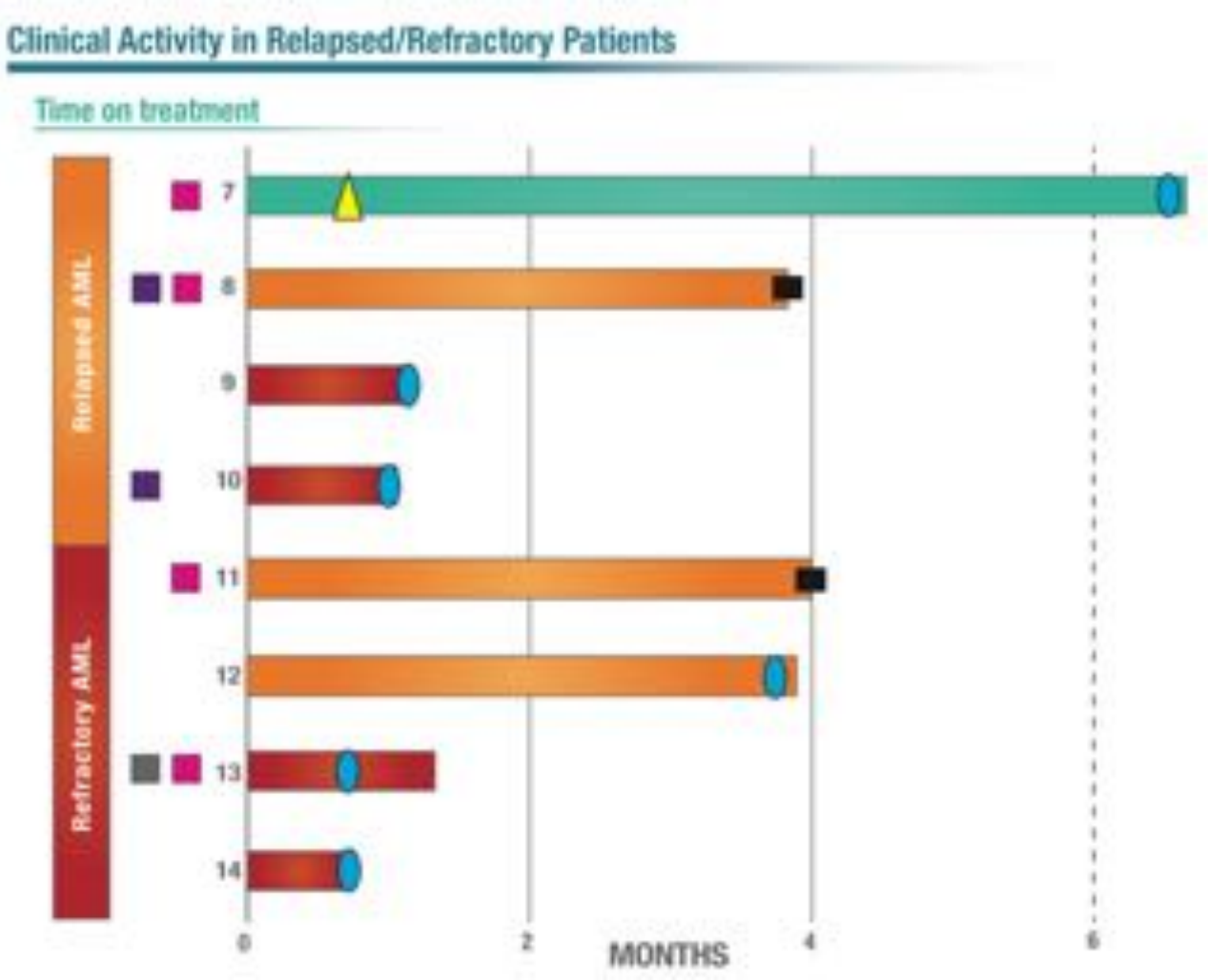
BerGenBio

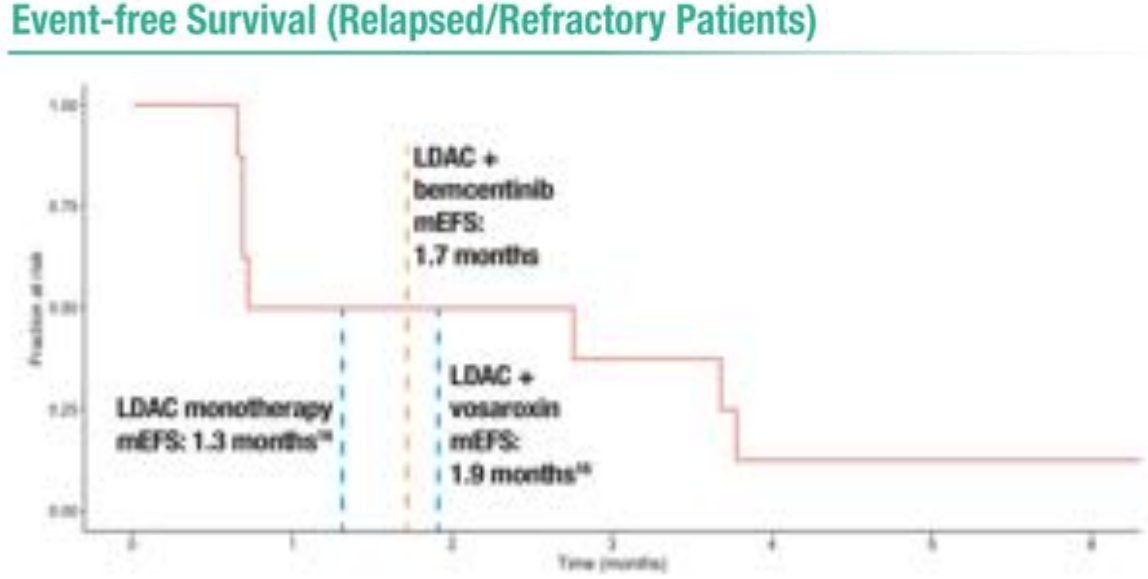
Bemcentinib + LDAC combination is active and effective in 1L newly diagnoses unfit/elderly AML patients

- 4/6 patients with ORR
- mDoR immature >12months and all 4 responding patients ongoing
- Responding patients have poor risk factors



Bemcentinib + LDAC in r/r AML patients





2L r/r AML LDAC combo expansion cohort 28pts ongoing

BerGenBio

Registration strategies for bemcentinib in AML under consideration

Bemcentinib has FAST TRACK DESIGNATION by FDA in AML.

3 possible registration paths are apparent, in slightly different patient populations

Scientific advice will be sort early 2020, route to registration to be discussed

1. 2L Bemcentinib + LDAC combination

- relapse patients >60 years, patients having failed HMA or HMA+Venetoclax
- rPh II / III, to receive bem+LDAC or LDAC alone
- End points: ORR and DoR
- Anticipated sample size 200 with 6 month f/u

2. ≥2L bemcentinib mono therapy

- Heavily pre-treated, ≥2L relapse patients >75yrs, with low sAXL
- sAXL assay is a CLSI validate Clinical Trial Assay method performed at a CLIA lab.
- Possible single arm or comparator being best supportive care (BSC) or palliative care
- End points: ORR and DoR
- Anticipated sample size 100 with 6 month f/u

3. 1L Bemcentinib + LDAC combination

- 1L patients >60 yrs, unsuitable for HMA+Venetoclax
- rPh II / III
- End points: ORR and DoR/OS
- Anticipated sample size 200 with 12 month f/u

Ref. BGBC008 / NCT03184571

Bemcentinib clinical development in Non Small Cell Lung Cancer (NSCLC)

Objective: to improve the effectiveness of immune check point inhibitor (CPI) (pembrolizumab/Keytruda) refractory NSCLC patients, with a well tolerated, effective, and convenient drug

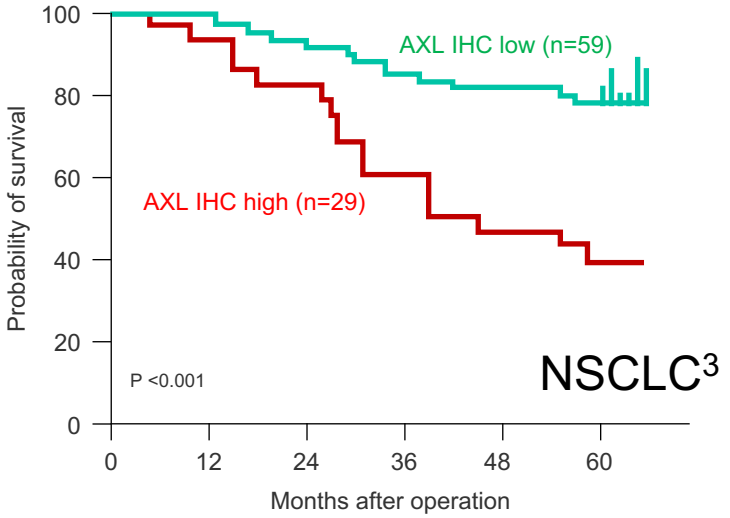
Chemotherapy refractory patients

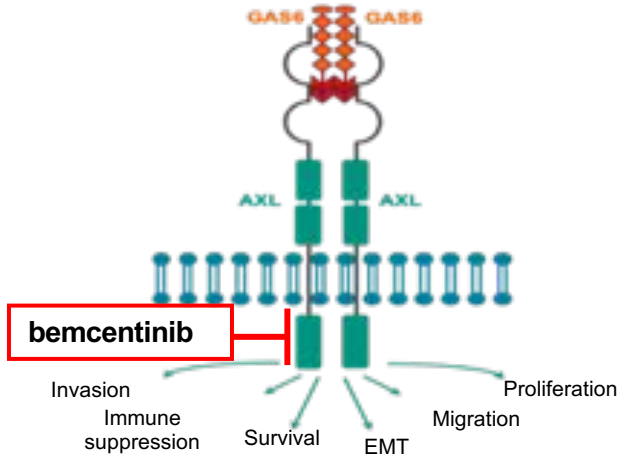
CPI +/- chemotherapy refractory patients

CPI+Chemotherapy refractory patients

Rationale for AXL inhibitor bemcentinib as an immuno-oncology agent in combination with check point inhibitor (CPI)

- AXL drives tumor EMT and resistance to cytotoxic lymphocyte-mediated cell killing[1]
- AXL receptor tyrosine kinase is a negative prognostic factor for many cancers including NSCLC[2]
- AXL expression is associated with anti-PD-1 therapy failure in melanoma patients[3]
- AXL is expressed by suppressive tumor-associated M2 macrophages and dendritic cells[4]
- Bemcentinib is a first-in-class highly selective, potent, and orally bioavailable, small molecule AXL kinase inhibitor
- Bemcentinib reverses EMT, repolarizes TAMs and potentiates efficacy of immunotherapy in murine cancer models[4]





[1]Terry, 2019; [2]Hugo, 2016; [3]Ishikawa, 2012, Davidsen,2017; [4]Ludwig, 2018, Davidsen, submitted

NSCLC causes more cancer related deaths than breast, colon, pancreas and prostate combined

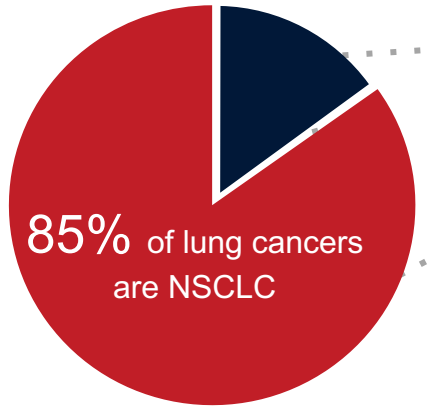
The largest cancer killer, most patients depend on drug therapy

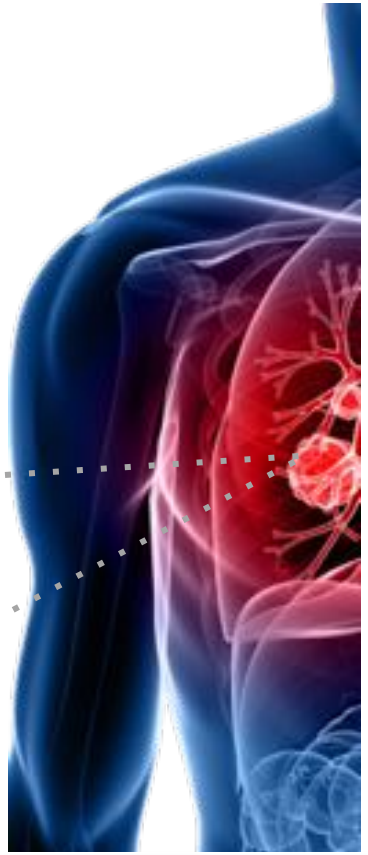
The most common type of cancer

2.09 million new cases of lung cancer diagnosed/yr worldwide, making up 11.6% of all cancer cases[1]

1.76 million lung cancer deaths/yr worldwide[1]

5-year survival rate is 3.5% in patients with PD-L1 <1%, and **12.6%** in patients PD-L1 1-49%

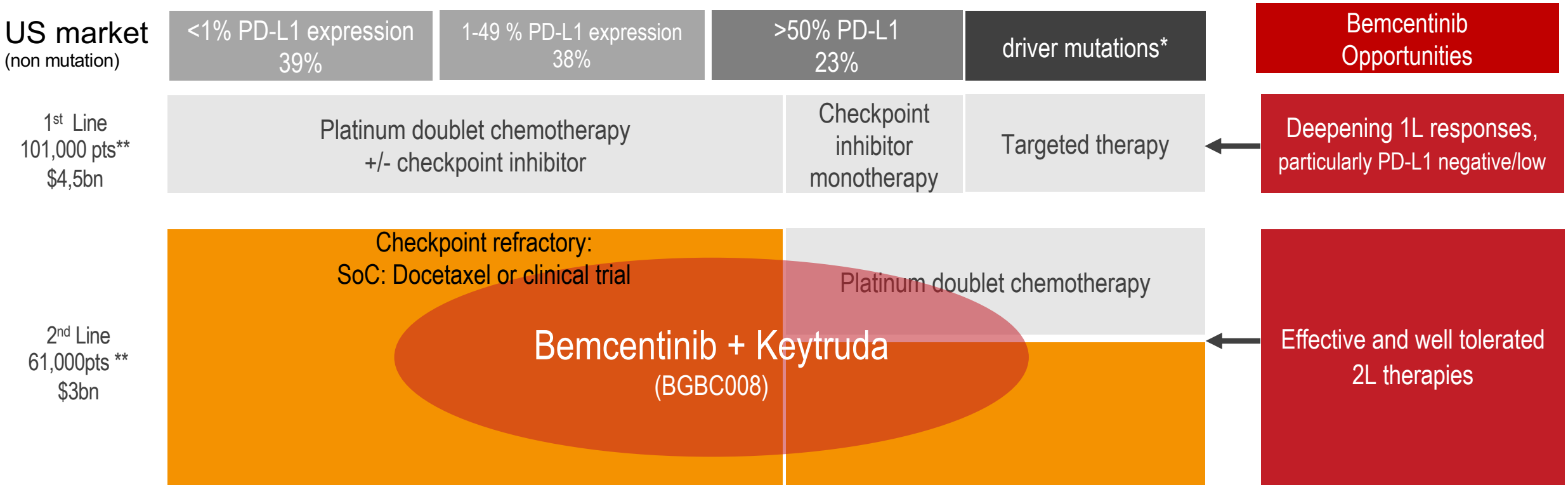




(1) fortunebusinessinsights.com/industry-reports/non-small-cell-lung-cancer-therapeutics-market-100484

Non- Small Cell Lung Cancer (NSCLC)

Rapidly evolving SoC creates opportunities for novel effective, chemo free well tolerated regimens



* Mutations / rearrangements with available targeted therapies such as EGFR and ALK
** Evaluate Pharma.USA only

Bemcentinib + KEYTRUDA in refractory/relapsed NSCLC

Phase II Study Design

BGBC008
Phase II 2-stage study of bemcentinib (BGB324) in combination with pembrolizumab

Inclusion criteria
- Adenocarcinoma histology
- Measurable disease
- Fresh tumor tissue
- AXL and PD-L1 All comers

Assessments
Efficacy
- **Primary endpoint**
  - Objective Response Rate
- **Secondary endpoints**
  - Duration of Response
  - Disease Control Rate
  - Time to Progression
  - Survival at 12 months
  - Response by Biomarker expression

Safety
PK

Regimen
- Pembrolizumab 200mg fixed
- Bemcentinib 400mg loading dose, then 200mg OD

Cohort A

- **Previously treated with a platinum containing chemotherapy**
- 2nd line advanced adeno NSCLC

Cohort B

- **Previously treated with a checkpoint inhibitor (PD-L1 or PD-1 inhibitor)**
- No more than 2 previous lines of treatment
- Must have had disease control for ≥12 weeks followed by progression
- 2nd or 3rd line advanced adeno NSCLC

Cohort C

- **Previously treated 1st line with a checkpoint inhibitor- containing regimen in combination with a platinum-containing chemotherapy**
- Disease control on 1st line therapy for ≥12 weeks followed by progression
- 2nd line advanced adeno NSCLC

Interim Analysis

Stage 1

N=24 patients

(each patient has the potential for at least 24 weeks follow-up)

Stop at this stage for:
Futility (H0:15% if ≤3 responses)
Or unfavorable risk/benefit

Interim Analysis Cohorts B & C

Stage 1

N=13 patients/cohort

(each patient has the potential for at least 24 weeks follow-up)

Stop at this stage for
Futility (H0:15% if 0 responses)
Or unfavorable risk/benefit

Final Analysis

Stage 2

N=50 patients total

(each patient has the potential for at least 24 weeks follow-up)

Final Analysis Cohorts B & C

Stage 2

N=29 patients/cohort

(each patient has the potential for at least 24 weeks follow-up)

Ref. BGBC008 / NCT03184571 – clinical trial collaboration with Merck & Co., Inc.

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PK

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COMPLETED: INFORMS 1L OPPORTUNITY

Cohort A
- Previously treated with a platinum containing chemotherapy
- 2nd line advanced adeno NSCLC

Interim Analysis
Stage 1
N=24 patients
(each patient has the potential for at least 24 weeks follow-up)

Stop at this stage for:
Futility (H0:15% if ≤3 responses)
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Final Analysis
Stage 2
N=50 patients total
(each patient has the potential for at least 24 weeks follow-up)

Cohort B
- **Previously treated with a checkpoint inhibitor (PD-L1 or PD-1 inhibitor)**
- No more than 2 previous lines of treatment
- Must have had disease control for ≥12 weeks followed by progression
- 2nd or 3rd line advanced adeno NSCLC

Cohort C
- **Previously treated 1st line with a checkpoint inhibitor- containing regimen in combination with a platinum-containing chemotherapy**
- Disease control on 1st line therapy for ≥12 weeks followed by progression
- 2nd line advanced adeno NSCLC

Interim Analysis Cohorts B & C
Stage 1
N=13 patients/cohort
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Final Analysis Cohorts B & C
Stage 2
N=29 patients/cohort
(each patient has the potential for at least 24 weeks follow-up)

Ref. BGBC008 / NCT03184571 – clinical trial collaboration with Merck & Co., Inc.

Cohort A Patient Disposition and Demographics*

Patient disposition	N
Screened	74
Enrolled	50
Evaluable	44
Ongoing	9

Patient demographics		N (%)
Age	Median	65
	Range	39-82
ECOG at screen	0	22 (44%)
	1	28 (56%)
Sex	Female	20 (40%)
Smoking Status	Smoker	10 (20%)
	Ex-smoker	29 (58%)
	Never smoked	10 (20%)
	Unknown	1 (2%)

Disease mutations	N (=50)
None	36 (72)
KRAS	7 (14)
TP53	2 (4)
EGFR	3 (6)
Other	4 (8)

Safety Summary

The safety profile of combination treatment is consistent with that of each individual drug

Treatment related adverse events were generally mild and reversible

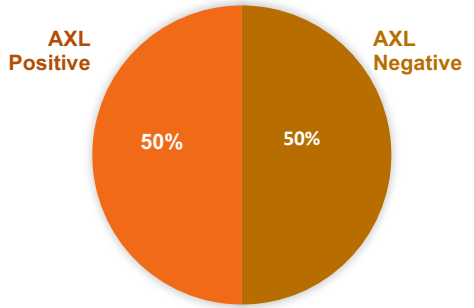
Treatment related adverse events were considered to be less severe and better tolerated than for other TKIs or CPI combinations used in NSCLC

Most frequent TRAEs (≥10% dosed pts)

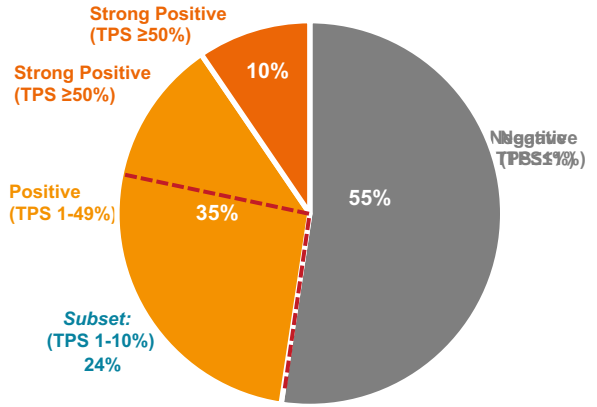
Event Terms	All Grades		Grade≥3	
	n	%	n	%
Transaminase increased*	19	38 %	7	14%
Asthenia / Fatigue	15	30 %	4	8%
Diarrhoea	12	24 %	0	0%
Nausea	7	14 %	0	0%
Anaemia	6	12 %	1	2%
Blood creatinine increased	6	12 %	0	0%
Decreased appetite	6	12 %	0	0%
Pruritus	5	10 %	0	0%

Biomarker

cAXL status
n = 30



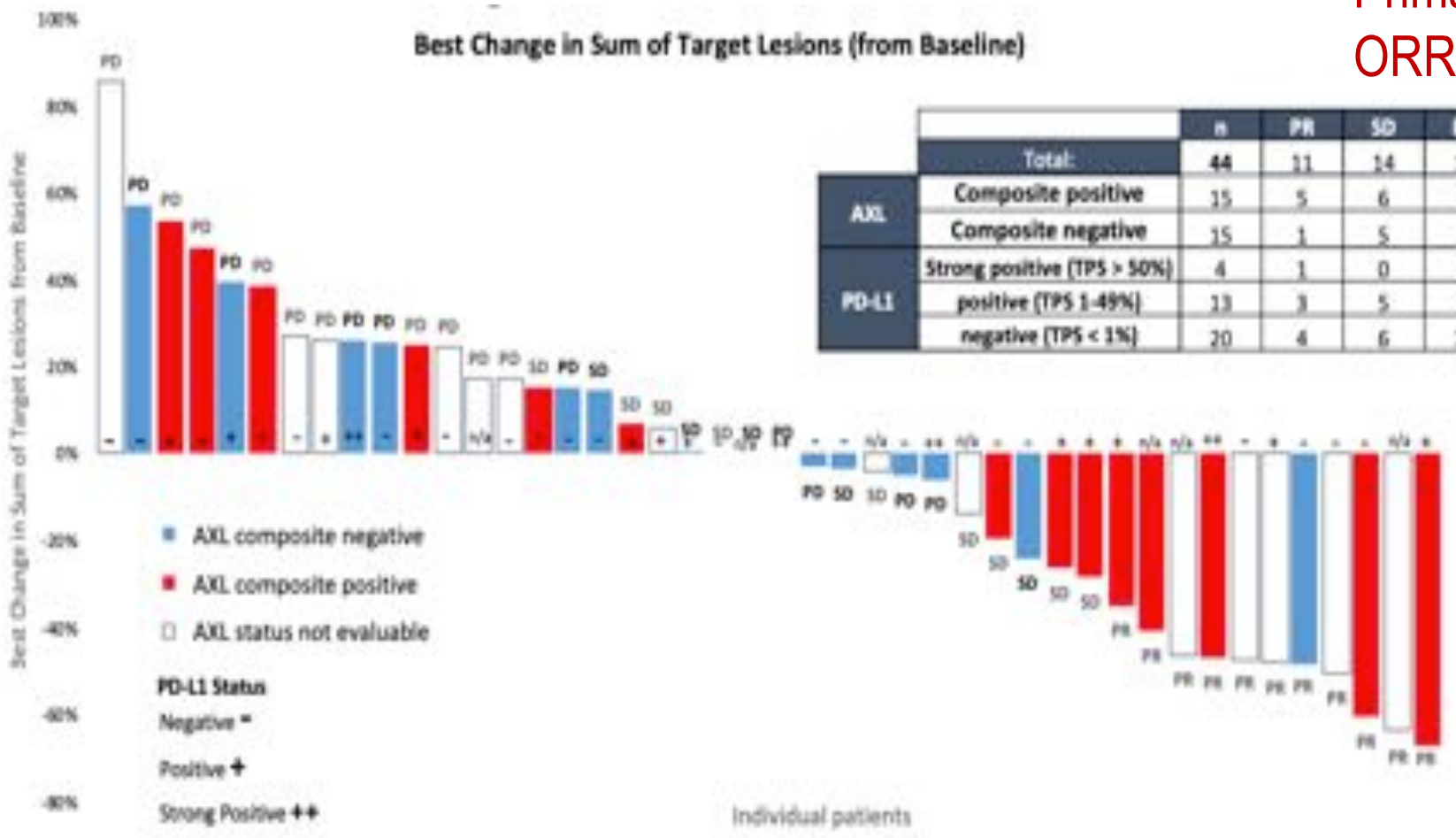
PD-L1 status
n = 37



*Data cutoff (30 Sep 2019)

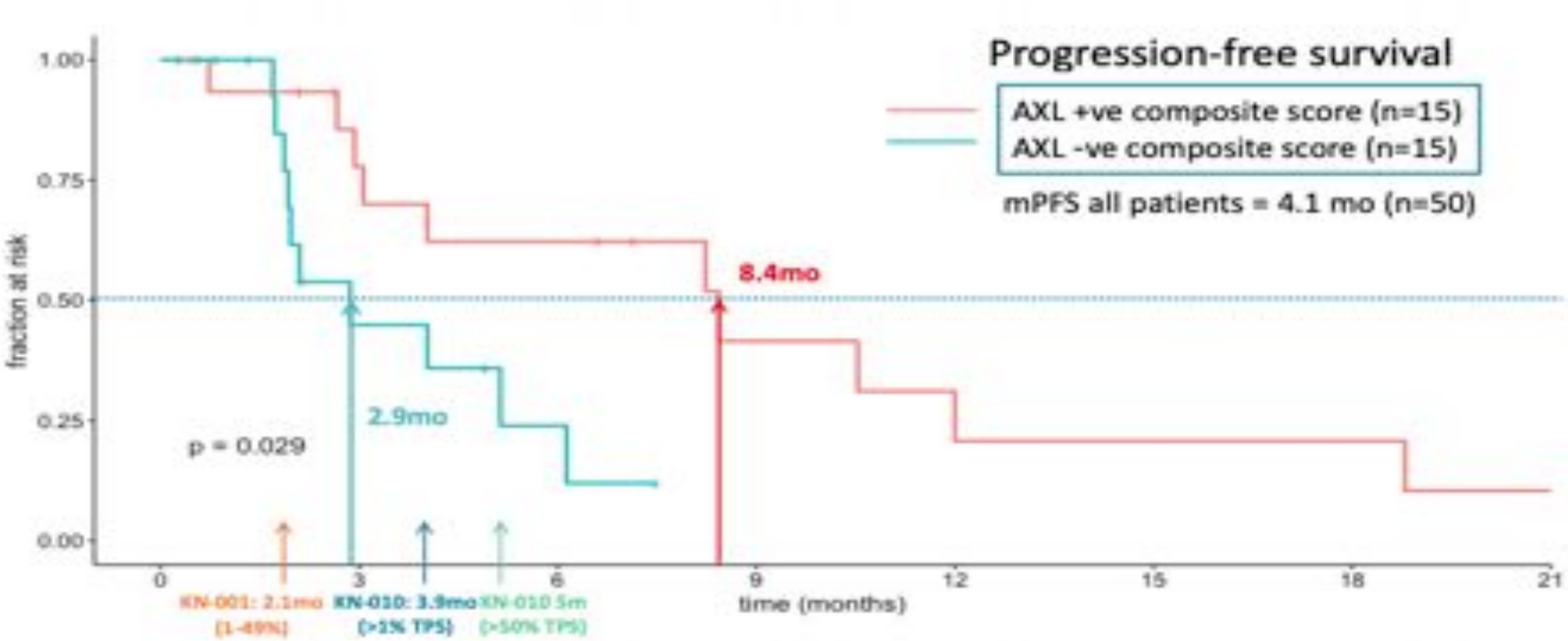
Anti-tumor activity of bemcentinib in combination with pembrolizumab: Change in tumour size from baseline by RECIST 1.1

Primary endpoint met:
ORR cAXL^{+ve} 5X > cAXL^{-ve}



		n	PR	SD	PD	ORR%	DCR%
	Total:	44	11	14	19	25	57
AXL	Composite positive	15	5	6	4	33	73
	Composite negative	15	1	5	9	7	40
PD-L1	Strong positive (TPS > 50%)	4	1	0	3	25	25
	positive (TPS 1-49%)	13	3	5	5	23	62
	negative (TPS < 1%)	20	4	6	10	20	50

Significant mPFS improvement in cAXL +ve patients:
AXL is an adverse prognostic biomarker – therefore cAXL score is predictive



- ✓ 3-fold improvement in cAXL +ve vs. cAXL –ve patients.
- ✓ 4-fold improvement in what might be expected in the same patient population with Keytruda monotherapy

Source: KN001; Garon *et al* NEJM 2015; KN-010 Herbst *et al*, Lancet 2016

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- 2nd or 3rd line advanced adeno NSCLC

Cohort C
- Previously treated 1st line with a checkpoint inhibitor- containing regimen in combination with a platinum-containing chemotherapy
- Disease control on 1st line therapy for ≥12 weeks followed by progression
- 2nd line advanced adeno NSCLC

Interim Analysis
Stage 1
N=24 patients
(each patient has the potential for at least 24 weeks follow-up)

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Futility (H0:15% if ≤3 responses)
Or unfavourable risk/benefit

Final Analysis
Stage 2
N=50 patients total
(each patient has the potential for at least 24 weeks follow-up)

Interim Analysis Cohorts B & C
Stage 1

N=13 patients/cohort

(each patient has the potential for at least 24 weeks follow-up)

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Futility (H0:15% if 0 responses)
Or unfavourable risk/benefit

Final Analysis Cohorts B & C
Stage 2

N=29 patients/cohort

(each patient has the potential for at least 24 weeks follow-up)

ONGOING
WILL INFORM 2L PIVOTAL STUDY

Ref. BGBC008 / NCT03184571 – clinical trial collaboration with Merck & Co., Inc.

MERCK

Bemcentinib + KEYTRUDA in refractory/relapsed NSCLC – cohort B & C

CHECK POINT INHIBITOR REFRACTORY PATIENTS: precise and specific definition

Patients must have reported an initial clinical benefit (CR, PR or SD) for at least 12 weeks and subsequently progressed on treatment with an anti-PD1/L1 monoclonal antibody (mAb) administered either as monotherapy, or in combination with other checkpoint inhibitors or other therapies. PD-1 treatment progression is defined by meeting all of the following criteria:

a) Has received at least 2 doses of an approved anti-PD-1/L1 mAb.

b) Has demonstrated disease progression after PD-1/L1 as defined by RECIST v1.1. The initial evidence of disease progression (PD) is to be confirmed by a second assessment no less than four weeks from the date of the first documented PD, in the absence of rapid clinical progression.

c) Progressive disease has been documented within 12 weeks from the last dose of anti-PD-1/L1 mAb. Seymour et al; iRECIST: Guidelines for response criteria for use in trials testing immunotherapeutics. Lancet Oncol 18: e143-52

This determination is made by the investigator. Once PD is confirmed, the initial date of PD documentation will be considered the date of disease progression.

a) Other therapies not to be administered between last dose of anti PD-1/L1 mAb and commence of clinical trial agent

Interim Analysis Cohort B
Stage 1
N=13 patients/cohort

(each patient has the potential for at least 24 weeks follow-up)

- Stop at this stage for Futility (H0:15% if 0 responses)
- Or unfavourable risk/benefit

Lung Cancer
Clinical Development plan

BerGenBio

Development strategy for Bemcentinib in NSCLC (ad. & Sc.)

Clinical Position	Patient Population	Concept	Development Plan – target conditional approval / BT
2L IO(+chemo) refractory	Stage III/IV Ad. PD-L1 all comer cAXL +ve.	Randomised Phase IIb / III Bemcentinib + CPI vs. docetaxol 1º endpoints: Interim mPFS, (for C/A A) 6 & 12mn OS, OS (for full approval) 2º endpoints: ORR, DoR, Safety, tolerability.	1. Pending BGBC008 cohort B + C 2. SA advice from FDA & EMA 3. cAXL assay validation in BGBC008 B&C
1L	TBA		

BerGenBio

BGB149
anti-AXL monoclonal antibody

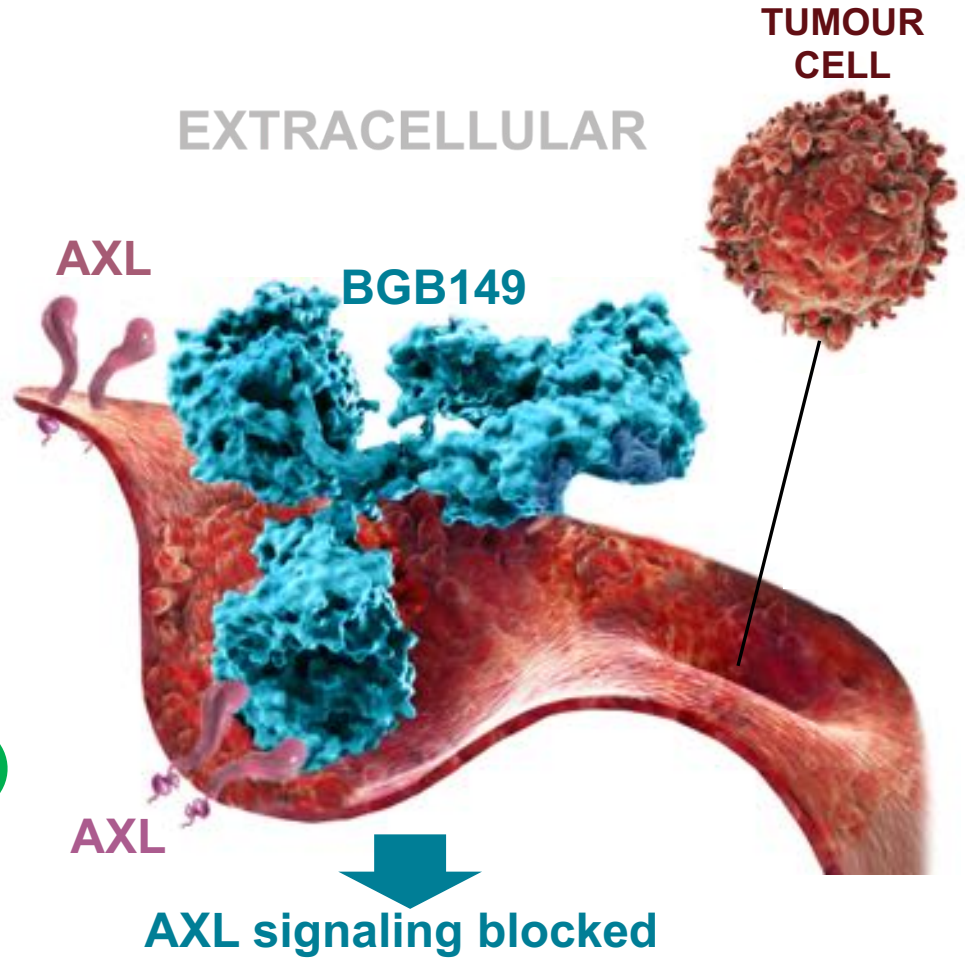
Ref. BGB149-101 / NCT03795142

BGB149: Anti-AXL monoclonal antibody

Phase I clinical trial ongoing

- Functional blocking fully-humanised IgG1 monoclonal antibody
- Binds human AXL, blocks AXL signalling
- High affinity (KD: 500pM), Anti-tumour efficacy demonstrated *in vivo*
- Robust manufacturing process established, 18 months stability
- Phase Ia healthy volunteer SAD study complete

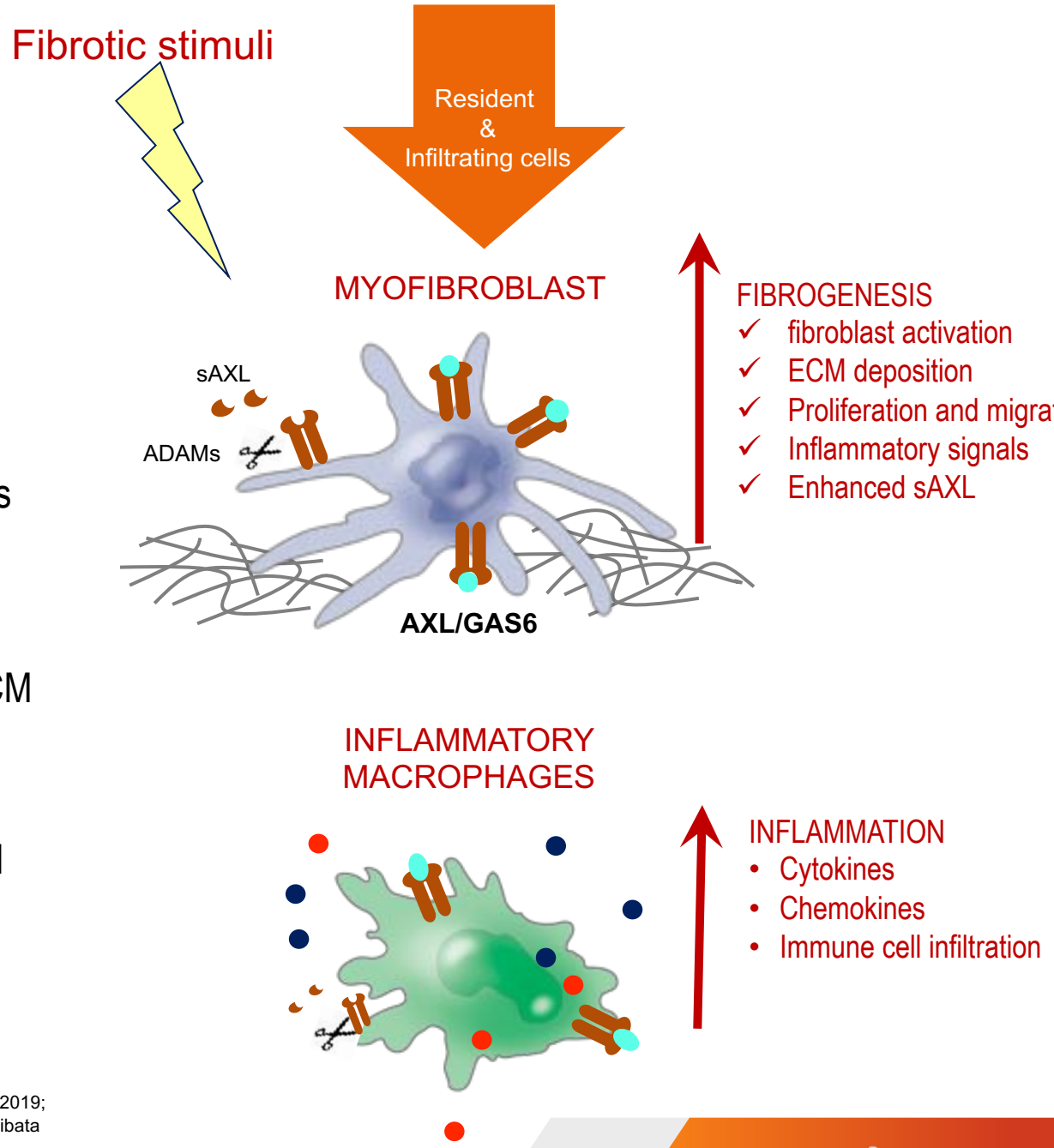
  Safety – no dose limiting toxicity seen up to 3mg/kg dose
  Pharmacokinetics - exposure predictable with dose proportional Cmax increase
  Confirmatory evidence of *in* vivo target engagement with sAXL -- stabilisation in circulation
- First-in-patient trial expected in H2 2019



BerGenBio

The role of AXL in fibrosis

- AXL Regulates and modulates key fibrogenic pathways
  - TGFb signaling[1,2]
  - Mechanosensing Hippo pathway[3]
  - Peroxisome proliferator-activated receptor[4]
- Axl regulates cellular plasticity implicated in fibrotic pathologies e.g. EMT, EndMT, Macrophage polarity
- AXL is a negative regulator of epithelial cell barrier integrity[5]
- Axl is required for hepatic stellate cell (HSC) activation and ECM deposition[6]
- Pharmacological modulation of Axl inhibits pre-clinical development of Liver ($CCl4_6$/HighFatDiet[7]), Renal (UUO_8) and Pulmonary (Asthma[9], Bleo[10], IPF[10]) fibrosis

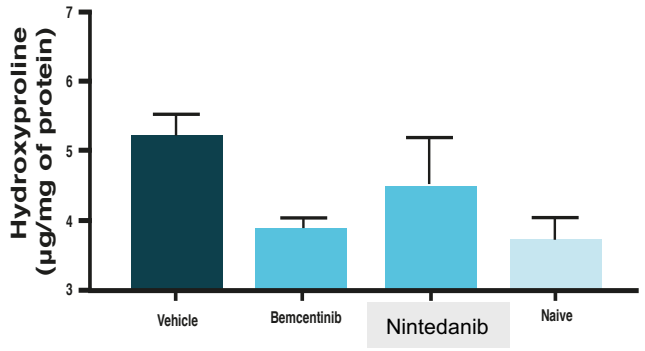


1 Gilbane ART 2015; 2 Reichl Hep. 2015; 3 Gibault ChemMed 2017; 4 Zhu AJTR 2016; Fuijno Lab invest 2017, J Exp Med 2019; 6 Barcena J. Hep 2015; 7 Tutusaus A. Cell Mol Gastroenterol 2019 Hepatol. 2019; 8 Landolt L. Physiol Reports 2019; 9 Shibata J Immunology 2014; 10 BerGenBio ASA, unpublilshed; 11 Espindola MS. Am J Respir Crit Care Med 2018)

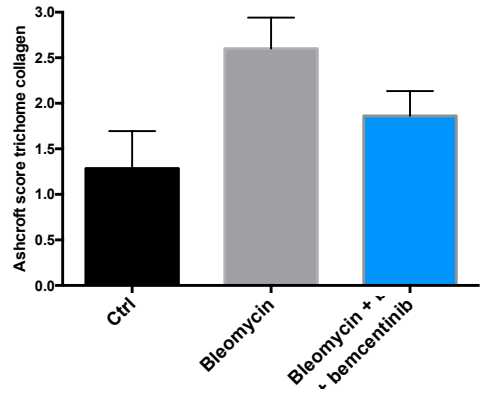
AXL inhibition prevents fibrosis in a panel of pre-clincial models

Lung

Bemcentinib reduces fibrosis in a human xenograft model of IPF [1]

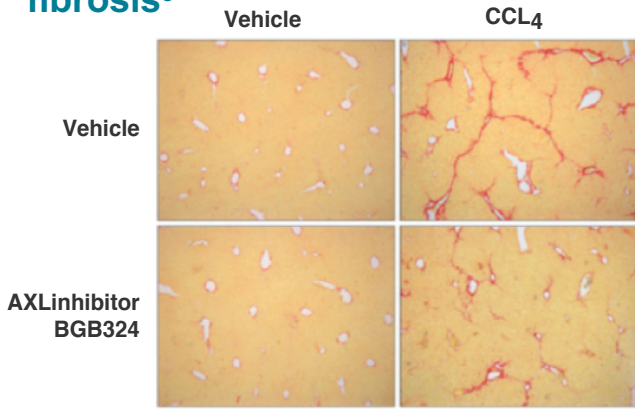


Bemcentinib reduces bleomycin induced fibrosis[2]

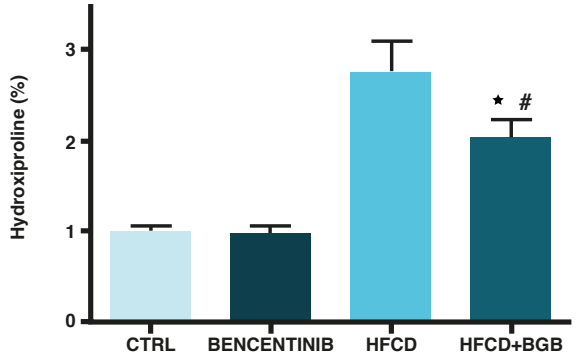


Liver

Bemcentinib reduces fibrosis in the CCL_4-induced model of liver fibrosis[3]



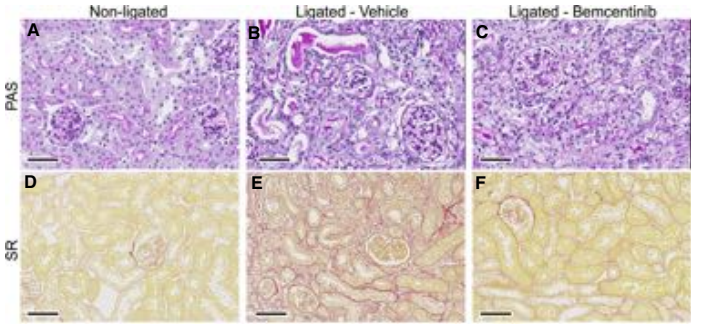
Bemcentinib reduces fibrosis in a diet induced model of NASH[4]



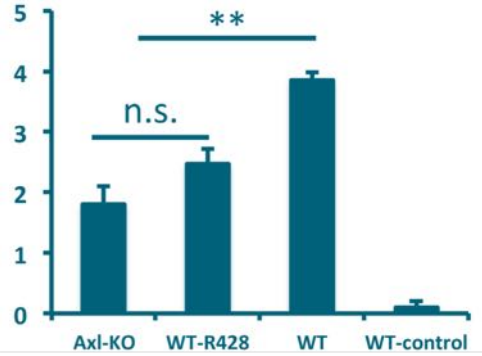
HFCD = high-fat, choline deficient diet
Leads to NASH in animal models

Kidney

Bemcentinib reduces kidney fibrosis following Unilateral Ureteral Obstruction (UUO) [5]



Bemcentinib ameliorates anti-GBM induced lupus like nephritis and improved kidney function [6]



1 Espindola et al., 2018; 2 BerGenBio ASA; 3 Barcena et al., 2015; 4 Tutsaus et al., unpublished; 5 Landolt et al., 2019 6 Zhen et al., 2018

BerGenBio

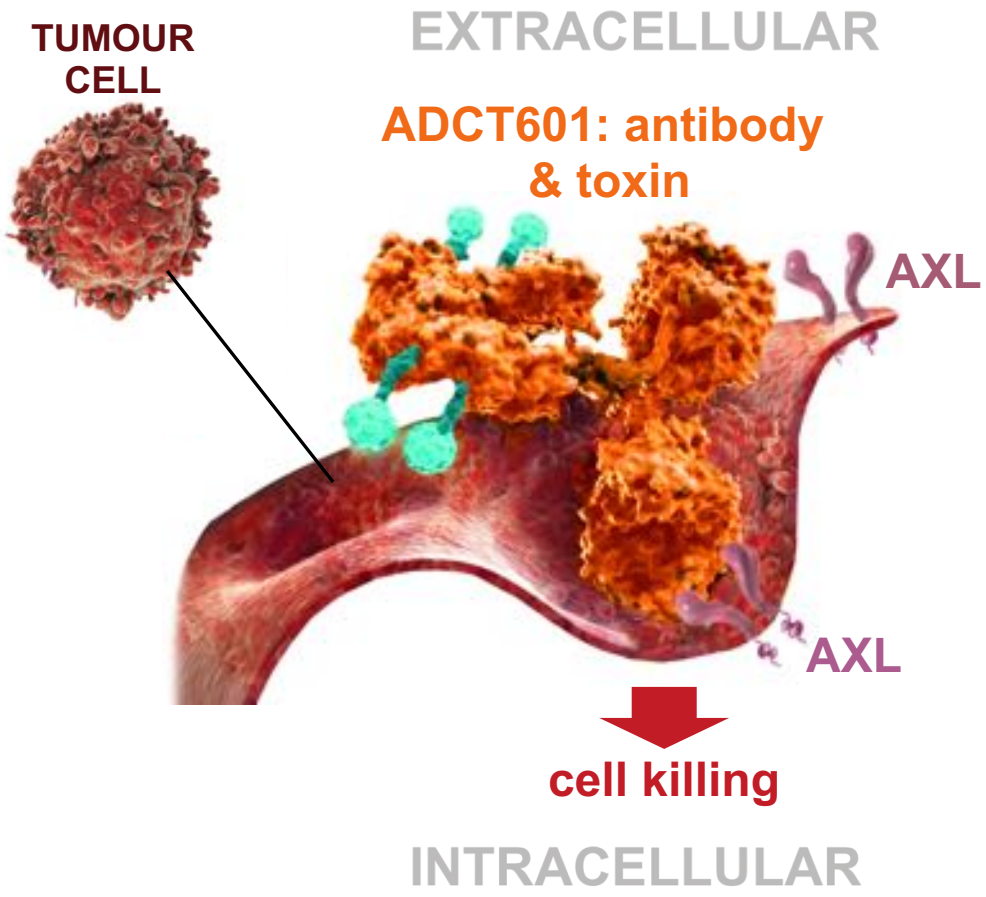
ADCT-601 – AXL ADC

Ref. NCT03700294

BGB601/ADCT-601: Anti-AXL ADC

Phase 1 in solid tumours ongoing

Out-licensed to ADC Therapeutics (ADCT)



Antibody Drug Conjugate (ADC)

Targets human tumour AXL, induces cell death when internalised

Potent and specific anti-tumour activity demonstrated preclinically[1]

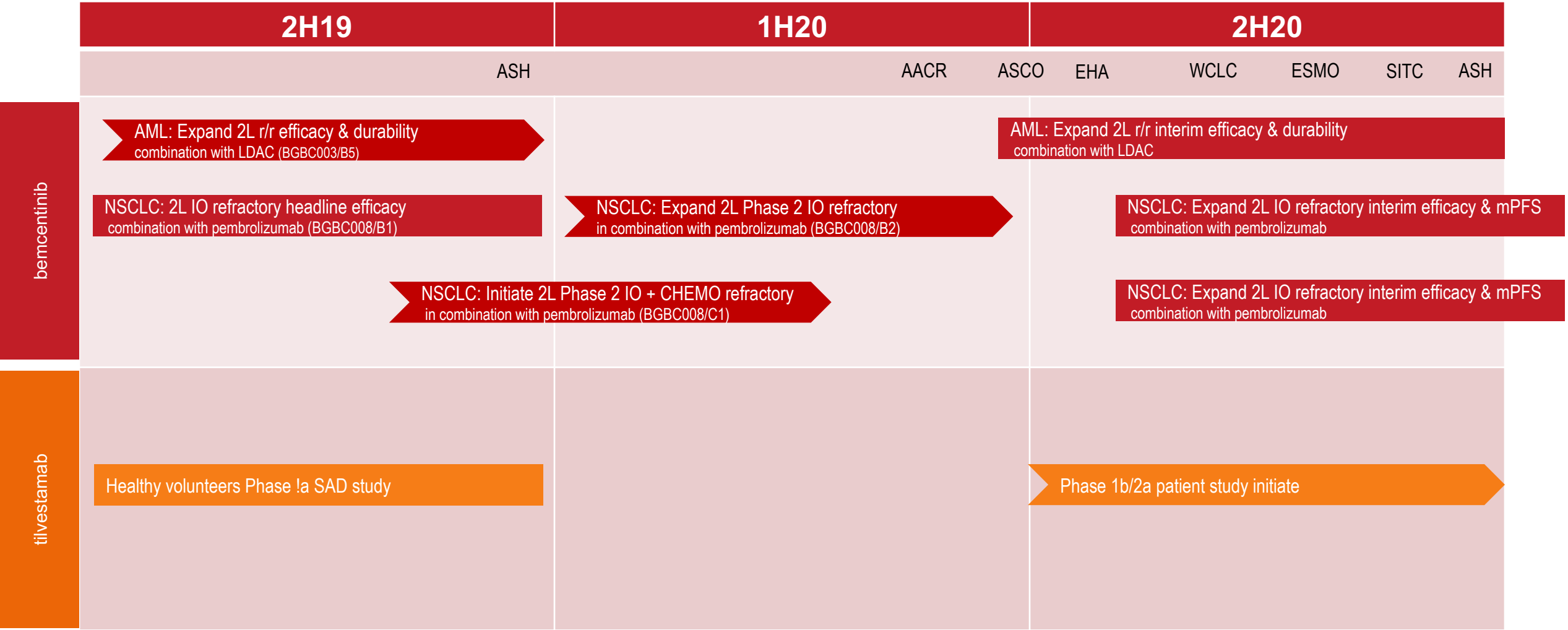
First-in-human Phase I study initiated in Jan 2019
- Solid tumours
- Up to 75 patients
- Safety, PK/PD, preliminary efficacy

Based on anti-AXL antibody BGB601 licensed from BerGenBio

(1) AACR 2018

Corporate

Expected Milestones Through 2020



Select Company Financials

Oslo Børs	BGBIO
Cash (Q3‘19)	$32m
Shares Outstanding	61,1m

Board of Directors

Sveinung Hole, Chairman of the board

- Non-Executive director of BerGenBio since 2010, chairman from 2019.
- Master of International Management.
- Representative of lead shareholder.

Prof. Stener Kvinnsland, MD.PhD Non-Executive Director

- Non-Executive director of BerGenBio since 2015
- More than 30 years of experience in oncology, Chair Oslo University Hospital, CEO of the Bergen Hospital Trust, Head of the Department of Oncology and Professor of Medicine (Oncology) at the University of Bergen and Director Clinical R&D, Oncology for Pharmacia & Upjohn in Milan.

Dr. Debra Barker MD, Non-Executive Director

- Non-Executive director of BerGenBio since 2019.
- Diploma in Pharmaceutical Medicine and MSc in immunology.
- Executive experience with Novartis, Roche, Smithkline Beecham and Knoll and served until recently as the Chief Medical and Development Officer at Polyphor Ltd.

Grunde Eriksen, Non-Executive Director

- Non-Executive director of BerGenBio since 2019.
- Experienced capital markets advisor and investor.
- 18 years international experience in corporate finance and equity sales with SEB & Arctic Securities

Dr. Pamela Trail, Noe-Executive Director

- Non executive director of BerGenBio since 2019.
- PhD from the University of Connecticut.
- Strategic oncology leadership roles at Regeneron, MedImmune, Bayer Healthcare and BMS and served as CSO at Seattle Genetics

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Link to reports from Trinity Delta:
https://www.bergenbio.com/investors/analyst-coverage/

Appendix

BerGenBio

Published papers in 2019 registered on Pubmed for AXL and Fibrosis: 8

Tutusaus *et a*l., (2019) Axl targeting abrogates experimental non-alcoholic steatohepatitis (NASH) progression, Cellular and Molecular Gastroenterology and Hepatology, In Press

- Bemcentinib reduces inflammation and fibrosis in a diet induced model of Non Alcoholoic Steato Hepatitis (NASH)
- Patients with advanced firbosis and cirrhosis have levated sAXL in circulation and AXL expression in liver biopsies.

Landolt *et al*., (2019) AXL targeting reduces fibrosis development in experimental unilateral ureteral obstruction. Physiol Rep

- Unilateral ureteric obstruction by ligation in mice, induced tubulointerstitial fibrosis with enhanced expression of AXL on cells of the interstitium, tubules and glomeruli
- Bemcentinib reduced development of fibrosis and inflammation in obstructed kidneys

Reviews

- **Bellan M, *et a*l. (2019) Gas6/TAM System: A Key Modulator of the Interplay between Inflammation and Fibrosis. Int J Mol Sci**
- **Smirne C, *et al*. (2019) Gas6/TAM Signaling Components as Novel Biomarkers of Liver Fibrosis. Dis Markers.**

COPD

Fujino *et al*., (2019) Sensing of apoptotic cells through Axl causes lung basal cell proliferation in inflammatory diseases. J Exp Med.

- Continued AXL signaling results in basal cell hyperplasia and a dysfunctional epithelial barrier in trachea with pathology typical of chronic inflammatory pulmonary diseases.
- Genetic depletion of AXL allows resolution of inflammation with differentiation to ciliated epithelium

Published papers in 2019 registered on Pubmed for AXL and Cancer: 122

Pearson et al., (2019) AXL Inhibition Extinguishes Primitive JAK2 Mutated Myeloproliferative Neoplasm Progenitor Cells.' HemaSphere 3.
- Inhibition of AXL with Bemcentinib preferentially kills early hemopoietic stem cells from patients with JAK2 mutated driven MPN

Terry et al., (2019) AXL Targeting Overcomes Human Lung Cancer Cell Resistance to NK- and CTL-Mediated Cytotoxicity, Cancer Immunology Research.
- AXL drives tumor EMT and resistance to cytotoxic lymphocyte-mediated cell killing
- Bemcentinib sensitizes NSCLC tumor cells to lymphocyte mediated cell killing

Cruz et al., (2019) Axl-mediated activation of TBK1 drives epithelial plasticity in pancreatic cancer. JCI Insight
- AXL drives an epithelial plasticity program enhancing invasive and metastatic capacity via TBK1 in KRAS-mutant PDA

Quinn et al., (2019) Therapeutic Inhibition of the Receptor Tyrosine Kinase AXL Improves Sensitivity to Platinum and Taxane in Ovarian Cancer. Mol Cancer Ther.
- AXL contributes to platinum and taxane resistance in ovarian cancer, and inhibition of AXL improves chemoresponse and accumulation of chemotherapy drugs

Tanaka et al., (2019) Axl signaling is an important mediator of tumor angiogenesis, Oncotarget.
- Bemcentinib decreases the secretion of pro-angiogenic factors and impairs functional properties of endothelial cells *in vitro* and *in vivo*

Tsukita et al., (2019) Axl kinase drives immune checkpoint and chemokine signalling pathways in lung adenocarcinomas. Mol Cancer.
- AXL positively correlates expressions of PD-L1 and CXCR6
- Bemcentinib decreased mRNA expressions of PD-L1 and CXCR6 in EGFR mutation-positive cell lines.

Reviews
- **Yan S, et al., AXL Receptor Tyrosine Kinase as a Therapeutic Target in Hematological Malignancies**: **Focus on Multiple Myeloma**. Cancers (Basel). 2019
- **Zhu C *et al*., AXL receptor tyrosine kinase as a promising anti-cancer approach: functions, molecular mechanisms and clinical applications.** Mol Cancer. 2019
- **Arner EN *et al*., Behind the Wheel of Epithelial Plasticity in KRAS-Driven Cancers.** Front Oncol.
- **Myers KV *et al*., Targeting Tyro3, Axl and MerTK (TAM receptors): implications for macrophages in the tumor microenvironment**. Mol Cancer.
- **Niu ZS *et al*., Role of the receptor tyrosine kinase Axl in hepatocellular carcinoma and its clinical relevance.** Future Oncol

References

Bemcentinib:

Ludwig, K.F.,*et al.,*(2017) Small molecule Axl inhibition targets tumor immune suppression andenhances chemotherapy in pancreatic cancer,' Epub ahead of print.

- Axl associated with poor outcomes in pancreatic cancer uniquely links drug resistance andimmune evasion.
- Bemcentinib blocks aggressive traits of pancreatic cancer&enhances activity of gemcitabine.
- Bemcentinib drives tumour cell differentiation and provokes an immune stimulatory microenvironment. Treatment reduces expression of Arginase-1 a key player in immune-suppression.

Guo et al (2017) Axl inhibition induces the antitumor immune response which can be further potentiated by PD-1 blockade in the mouse cancer models, Oncotarget

- Axl inhibition via bemcentinib reprograms immunological microenvironmentoIncreased proliferation and activation of CD4 and CD8
- Bemcentinib and PD-1 blockade act synergistiaclly

Mode of Action & Biomarkers

Haaland, G.S.,*et al.,*(2017) 'Association of warfarin use with Lower overall cancer incidenceamong patients older than 50 years,'*JAMA Intern Med*., Nov 6.

- Warfarin inhibits Axl signalling and Axl-mediated biological response at doses lower than thosewhich mediate anti-coagulation effects.
- Retrospective analysis of a large population cohort demonstrates that patients on low doseWarfarin had a significantly lower incidence of cancer.

Aguilera, T.A.&Giaccia, A.J. (2017) 'Molecular Pathways: Oncologic Pathways and Their Role inT-cell Exclusion and Immune Evasion-A New Role for the AXL Receptor Tyrosine Kinase,'*Clin.Cancer Res.,*June 15th.

- Immune checkpoint inhibitors are most effective against T-cell inflamed tumours. Non-T-cell or T-cell excluded tumours remain a significant barrier to treatment.
- Axl identified as a key mediator of immune evasion and experimental evidence demonstrates Axltargeting leads to greater anti-tumour immune response post radiotherapy.

Miller, M.A.,*et al.,*(2017) 'Molecular Pathways: Receptor Ectodomain Shedding in Treatment,Resistance, and Monitoring of Cancer,' Cl*in. Cancer Res.,*Feb 1.

- Proteases known as sheddases cleave the extracellular domain of several receptor tyrosinekinases such as Axl generating soluble Axl (sAxl).
- Plasma levels of sAxl are predictive of patient response to standard of care BRAF&MEKinhibitor therapy and could be used for patient stratification strategies.

Antony et al (2017) The GAS6-AXL signaling network is a mesenchymal (Mes) molecular subtype–specific therapeutic target for ovarian cancer.*Science Signalling*

- Axl particularly abundant in ovarian cancer subtype designated as mesenchymal (Mes)
- Axl co-clustered cMET, EGFR, and HER2, producing sustained extracellular signal–regulated kinase (ERK) activation in Mes cells
- Bemcentinib reduced tumor growth in chick chorioallantoic membrane model.

Kanzaki, R.,*et al.,*(2017) 'Gas6 derived from cancer-associated fibroblasts promotes migration ofAxl-expressing lung cancer cells during chemotherapy,'*Nature Scientific Reports,*Sept 6th.

- Tumor stroma microenvironment (TME) is comprised of cancer-associated fibroblasts (CAFs)which influence cancer cells such as non-small cell lung cancer (NSCLC).
- In a murine model, NSCLC treated with cisplatin induced an up-regulation of Gas6.
- NSCLC line H1299 migrated in response to Gas6.
- The CAF cell line LCAFhertexpresses GAS6 and can promote H1299 cell migration.
- Conclusion- CAF derived GAS6 promotes migration of Axl-expressing lung cancers.

Reviews

Levin et al (2016) Axl Receptor Axis: A New Therapeutic Target inLung Cancer.*J Thoracic Oncol*
Chouaib et al (2014) Tumor Plasticity Interferes with Anti-Tumor Immunity. *Critical RevImmunology*
Gay et al (2017) Giving AXL the axe: targeting AXL in human malignancy.*BJC*
Brown et al (2016) Gene of the month: Axl.*BMJ*
Halmos et al (2016) New twists in the AXL(e) of tumor progression. *Science Signalling*

BerGenBio

References

Resistance

Zucca, L.E.,*et al.,*(2017) 'Expression of tyrosine kinase receptor AXL is associated with worseoutcome of metastatic renal cell carcinomas treated with sunitinib,'*Urol Oncol.,*Oct 3.

- Renal cell carcinoma (RCC) represents 2-3% of all cancers in the Western world.
- First line therapy is sunitinib (PDGF/VEGF TK inhibitor).
- 47% of RCC patients treated with sunitinib were +ve for Axl.
- Axl expression in sunitinib treated patients correlated with worse clinical outcome (13 months Vs 43 months survival).

Husain, H.,*et al.*, (2017) 'Strategies to Overcome Bypass Mechanisms Mediating ClinicalResistance to EGFR Tyrosine Kinase Inhibition in Lung Cancer,'*Mol. Cancer Ther.*, Feb 2017.

- Patient treated with EGFR based therapies develop resistance via multiple mechanisms.
- Resistant metastatic lung cancers exhibit increased AXL, EMT and PDL1 expression.

Elkabets et al (2015) AXL Mediates Resistance to PI3Ka Inhibition by Activating theEGFR/PKC/mTOR Axis in Head and Neck and Esophageal Squamous Cell Carcinomas.*CancerCell*

- Axl mediates persistent mTOR activation and upregulated in resistant tumors
- Combined treatment with PI3Ka and either EGFR, AXL, or PKC inhibitors reverts this resistance

Mak et al (2015) A patient-derived, pan-cancer EMT signature identifies global molecularalterations and immune target enrichment following epithelial to mesenchymal transition.*ClinCancer Res*

- EMT signature was developed based on 11 tumor types
- Axl frequently overexpressed in EMT tumors along with PD-L1, PD1, CTLA4, OX40L, and PDL2
- highlights the possibility of utilizing EMT status--independent of cancer type--as an additional selection tool to select patients who may benefit from immune checkpoint blockade

Zhang et al (2012) Activation of the AXL kinase causes resistance to EGFR targeted therapy in lung cancer. *Nature Genetics*

Mueller et al (2014) Low MITF/AXL ratio predicts early resistance to multiple targeted drugs inmelanoma

- high Axl in melanoma cells correlates with drug resistance
- BRAF and ERK inhibitors are more effective when using Axl inhibition

References

Non-Oncology

Pulmonary fibrosis

Fujino N. et al., (2017) Phenotypic screening identifies Axl kinase as a negative regulator of an alveolar epithelial cell phenotype. Lab Invest. 2017 Sep;97(9):1047-1062.

- Axl was activated in hyperplasia of epithelial cells in idiopathic pulmonary fibrosis patients where the epithelial barrier integrity was lost
- In vitro, Axl inhibition or downregulation by small interfering RNA led to increase in epithelial surfactant protein expression and promotion of an epithelial cell phenotype.

Espindola, M. S. et al., (2018) Targeting of TAM Receptors Ameliorates Fibrotic Mechanisms in Idiopathic Pulmonary Fibrosis. Am J Respir Crit Care Med 197, 1443–1456.

- IPF patients with high expression of Axl are rapid (declining lung function) progressors.
- Bemcentinib inhibited the fibrogenic phenotype of IPF patient derived fibroblasts.
- GAS6 knockout animals were protected from Bleomycin induced lung fibrosis (Gold standard model of pulmonary fibrosis).
- Bemcentinib inhibited the development of fibrosis in the IPF SCID mouse model (Human IPF fibroblasts induce pulmonary fibrosis in the SCID mouse).

Chronic Obstructive Pulmonary Disease

Fujino, N. et al., (2019) Sensing of apoptotic cells through Axl causes lung basal cell proliferation in inflammatory diseases. J Exp Med 216, 2184–2201.

- Basal epithelial cells in the trachea, express AXL and are activated by Gas6 ligand interaction with apoptotic cells in airway inflammation.
- AXL signaling is critical for expansion of the pool of basal cells, but needs to be silenced to allow differention of basal epithelium □ ciliated cell regeneration.
- Continued AXL signaling results in basal cell hyperplasia and a dysfunctional epithelial barrier with abnormal differentiation to squamous (not ciliated) epithelium and continued cell turnover, typical of the pathology of chronic inflammatory pulmonary diseases.
- Genetic depletion of AXL allows resolution of inflammation with differentiation to ciliated epithelium

Liver Fibrosis

Staufer K.,*et al.,*(2017) 'The non-invasive serum biomarker soluble Axl accurately detects advanced liver fibrosis and cirrhosis,'*Cell Death Dis.* Oct 26.

- sAxl confirmed to be accurate biomarker of liver fibrosis and cirrhosis.
- sAxl/albumin demonstrated to be further enhancing as a cheap and accurate biomarker.

Barcena et al (2015) Gas6/Axl pathway is activated in chronic liver disease and its targeting reduces fibrosis via hepatic stellate cell inactivation.*J Hepatology,* Sep;63(3):670-8

- Axl levels paralleled HSC activation
- Axl knock out mice displayed decreased HSC activation in vitro and liver fibrogenesis after chronic damage by CCl4 administration
- Bemcentinib reduced collagen deposition and CCl4-induced liver fibrosis in mice

Tutusaus *et al*., (2019) Axl targeting abrogates experimental non-alcoholic steatohepatitis (NASH) progression, Cellular and Molecular Gastroenterology and Hepatology, In Press

- Bemcentinib reduces inflammation and fibrosis in a diet induced model of Non Alcoholoic Steato Hepatitis (NASH)
- Patients with advanced firbosis and cirrhosis have levated sAXL in circulation and AXL expression in liver biopsies.

Kidney fibrosis

Landolt, L. et al., (2019) AXL targeting reduces fibrosis development in experimental unilateral ureteral obstruction. Physiol Rep May;7(10):e14091

- Progressive chronic kidney disease is typified by kidney fibrosis, typified by activated myofibroblast accumulation and deposition of extracellular matrix.
- Unilateral ureteric obstruction by ligation, in mice, induced tubulointerstitial fibrosis with enhanced detection of AXL on cells of interstitium, tubules and glomeruli
- Bemcentinib reduced development of fibrosis and inflammation in obstructed kidneys compared to treatment with an ACE-inhibitor

Polycthaemia Vera, Myelofibrosis (MyeloProliferative Neoplasms - MPN)

Pearson, S. et al., (2019) 'AXL Inhibition Extinguishes Primitive JAK2 Mutated Myeloproliferative Neoplasm Progenitor Cells.' HemaSphere 3.

- AXL is upregulated and activated in JAK2 associated MPNs
- Inhibition of AXL with Bemcentinib preferentially kills early hemopoietic stem cells from patients and, as such represents a promising therapeutic approach for JAK2 driven MPN

Reviews

Bellan M, et al. (2019) Gas6/TAM System: A Key Modulator of the Interplay between Inflammation and Fibrosis. Int J Mol Sci. Oct 12;20(20)

Smirne C, et al. (2019) Gas6/TAM Signaling Components as Novel Biomarkers of Liver Fibrosis. Dis Markers. Sep 8;2019:2304931.