BerGenBio ASA (OSE: BGBIO)

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BGBIO – Corporate Snapshot

World leaders in understanding AXL biology

AXL is a novel drug target to overcome immune evasion, therapy resistance & spread

AXL upregulates PDL1 on dendritic cells and blocks T-cell immunity

AXL inhibitors – potential cornerstone of cancer therapy

Pipeline opportunities in multiple cancers and fibrosis

3 selective AXL inhibitors in clinical development

Bemcentinib,
AXL-antibody BGB149, AXL ADCT601*

Monotherapy and combinations with immune-, targeted and chemotherapies

Biomarker correlation across programme, parallel CDx development

Phase II Proof of Concept
AML (monotherapy), **AML** (chemo-combo)
NSCLC (KEYTRUDA combo)

Resourced to deliver significant milestones

Listed on Oslo Børs: BGBIO

Clinical trial collaborations with Merck and leading academic centres

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

Q1'19 Cash USD 35.7m

*AXL antibody out licensed to ADC Therapeutics SA

Bemcentinib Phase II POC data

Monotherapy
ACUTE MYELOID LEUKEMIA
2L r/r elderly

- **Bemcentinib monotherapy**
- **ORR 43%**
  - **AXL +ve patients**
- **mDoR – 3.1mo. (5.5* mo.)**

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

Chemo combination
ACUTE MYELOID LEUKEMIKA
1L & 2L elderly r/r AML

- **Bemcentinib + low dose chemo combination (LDAC)**
- **ORR 46%**
  - **All comer patient population**
- **mDoR in CR/Cri 6.2 months**
  (range 0.7 – 9.6 / immature)
- **Early onset of response**

CPI* combination
LUNG CANCER
2L chemo relapse/IO naïve ad. NSCLC

- **Bemcentinib + Keytruda combination**
  - **92% pts low/zero PD-L1**
- **ORR 40%**
  - **AXL +ve patients**
- **mPFS**
  - **5.9mo.** (stage I only)
- **mOS**
  - **12.2mo** (stage I only)

*Check point Inhibitor

**pts with radiological assessment

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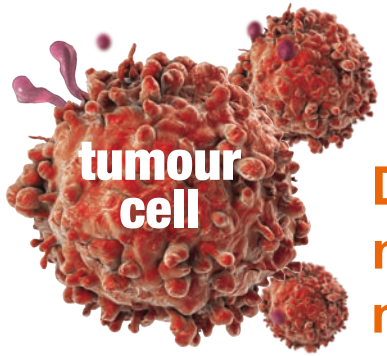
AXL drives aggressive cancer

AXL receptor tyrosine kinase drives aggressive disease including therapy resistant, immune-evasive tumours

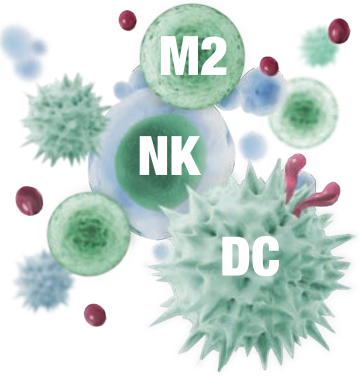


Drives tumour cell plasticity: non-genetic resistance mechanism

AXL drives features of aggressive cancer:

- Acquired therapy resistance
- Immune escape
- Metastasis

Key suppressor of innate immune response



AXL is an innate immune checkpoint:

- M1 to M2 macrophage polarisation
- Decreased antigen presentation by DCs
- Immunosuppressive cytokine profile

very **low** expression under healthy **physiological conditions** (ko mouse phenotypically normal)

overexpressed in response to **hypoxia, immune reaction, cellular stress** / therapy

overexpression correlates with **worse prognosis in most cancers**

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The role of AXL in I/O resistance

AXL is prevalent in TAMs

Pro-tumoural, immune-suppressive tumour associated macrophages (TAMs) are rich in AXL but not Mer (Jim Lorens lab, **unpublished data**)

↓Antigen presentation by DCs, NK cell activity

Paolino 2014 *et al* (2014) found that inhibition of AXL decreased NK cell activity and their ability to eliminate metastases.

Kurowska-Stolarska *et al* (2017) demonstrate that AXL acts as off-switch for DCs

↓T-cell mediated killing

Pre-treatment of mesenchymal tumour cells with bemcentinib increase T-cell mediated killing due to more efficient immunological synapse (Chouaib lab, **unpublished data).**

Sakemura *et al* reported at ASH 2018 that AXL targeting increases CAR-T therapy efficacy.

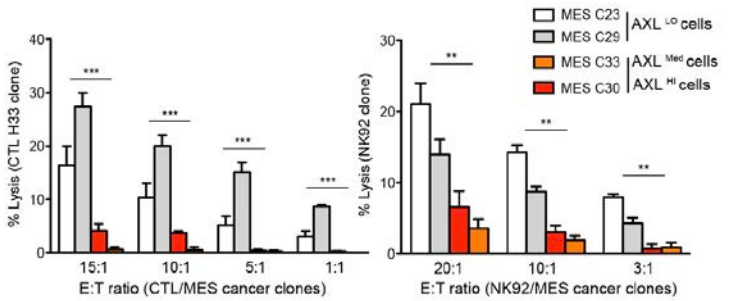
Resistance to PD-1 inhibitors in patients

Hugo *et* al Cell 2016: Identified a transcriptional signature related to innate anti-PD-1 resistance in melanoma: AXL is one of top differentially expressed genes in non-responders

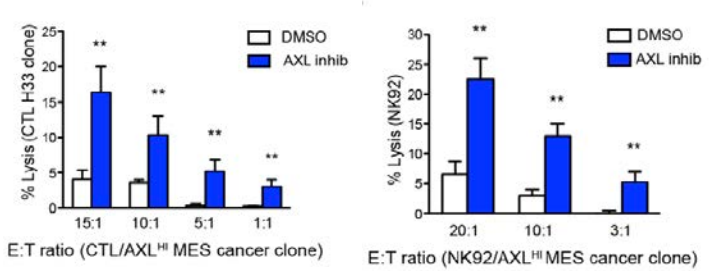
Preclinical data at AACR reinforces bemcentinib's potential to reverse tumour immunosuppression and therapy resistance

Chouaib *et al*

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



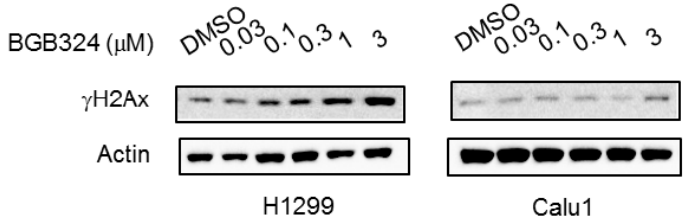
Bemcentinib treatment of the tumour cells with high AXL expression reverses this effect



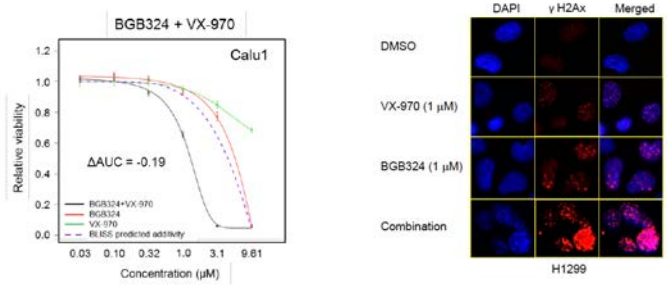
Key pre-clinical data supporting the rationale of combining bemcentinib with IO / bemcentinib's IO MoA

Ramkumar, Byers *et al*

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



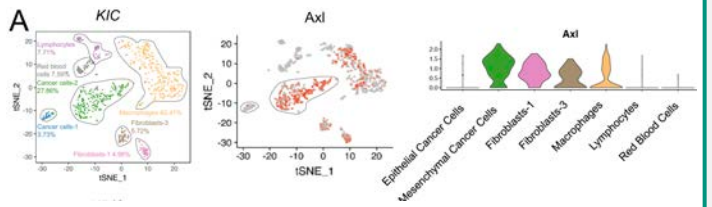
Bemcentinib has synergistic effect when given in combination with DNA damage targeting agents (VX-970)



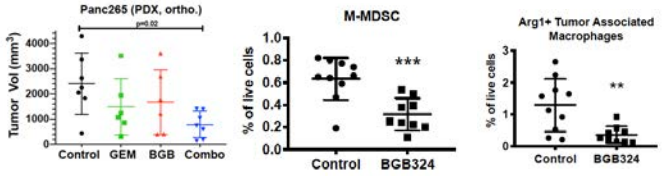
Supports the rationale of combining bemcentinib with chemo and DNA damaging agents

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

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Bemcentinib

Highly selective, potent, orally bioavailable AXL inhibitor

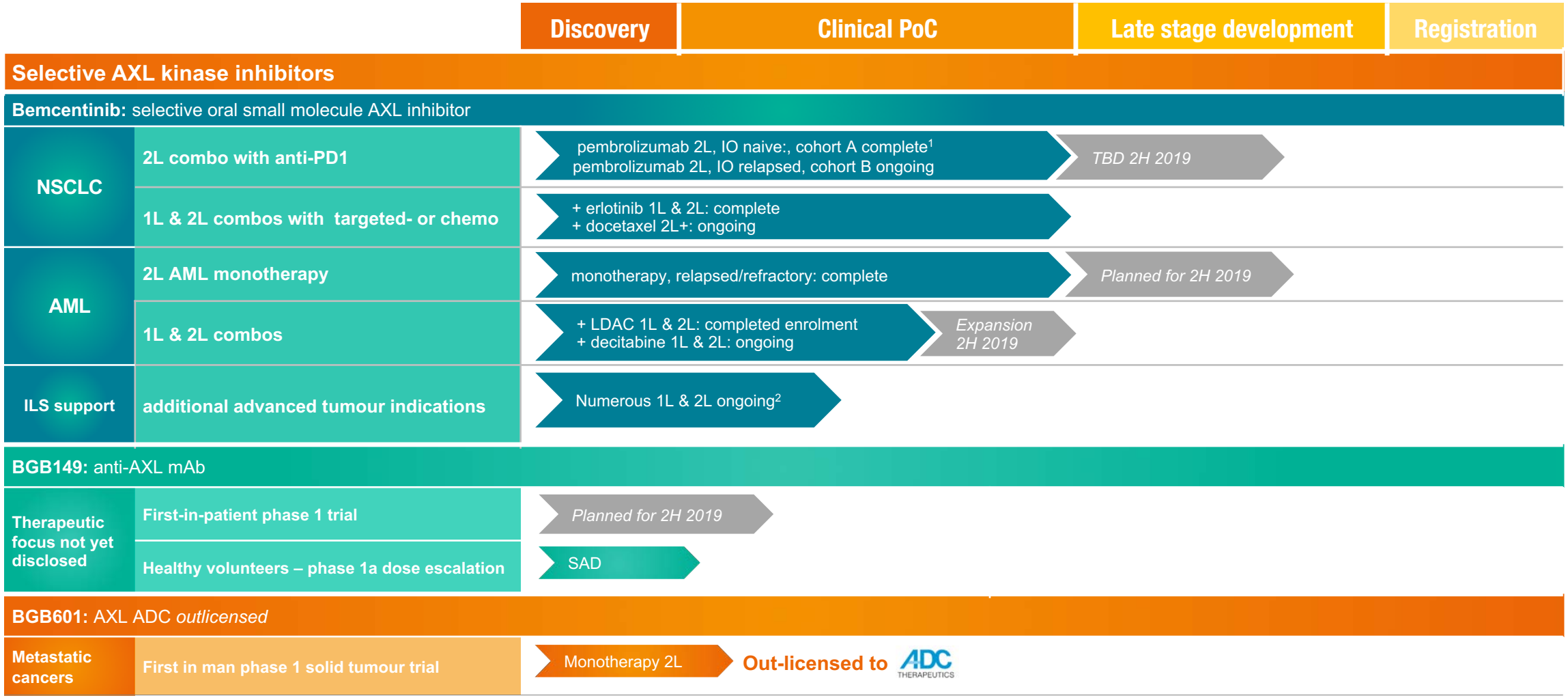
Bemcentinib: once-a-day pill

- Highly selective, potent, orally bioavailable
- Blocks AXL signalling, reverses aggressive tumour traits & counteracts immune escape
- Once-a-day administration
- Clinical PoC in AML and NSCLC as a monotherapy and in combination
- Correlation of clinical efficacy with AXL biomarkers observed
- Combines successfully with chemo, targeted and CPI drugs
- Excellent clinical safety profile: >250 subjects dosed

Phase II clinical proof of concept studies for bemcentinib

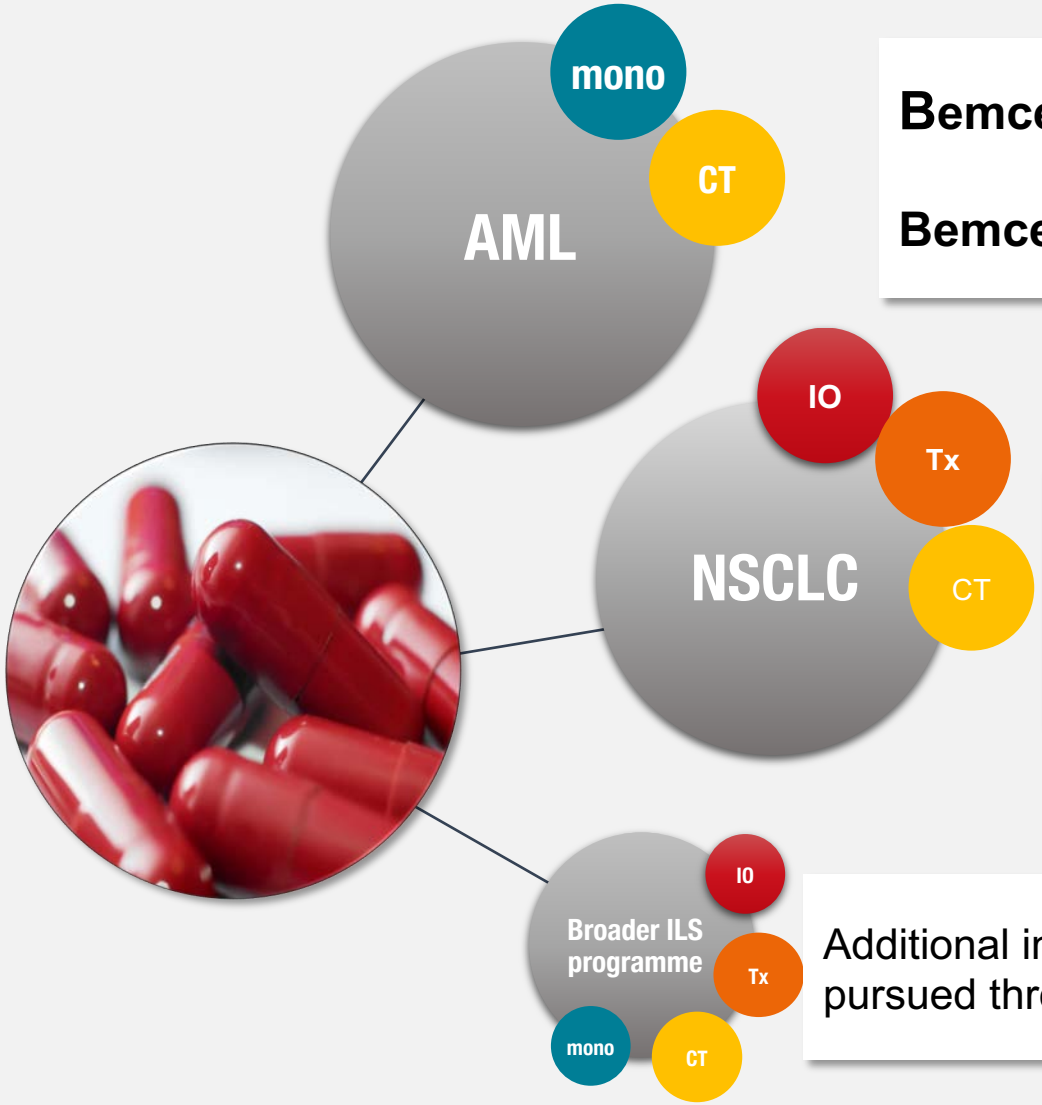
		Clinical Proof-of-concept	Late stage Opportunities
Monotherapy Selected, biomarker directed patients	AML / MDS	Completed	
	Glioblastoma (IIT)	Ongoing	
	Ovarian (EMT signature selected)	Potential	
Chemotherapy Combinations Improve responses in hard to treat settings	AML + LDCT (LDAC)	Ongoing	
	Pancreatic, (IIT)	Ongoing	
	NSCLC (IIT)	Ongoing	
Immunotherapy Combinations Target resistance, enlarge addressable patient population	NSCLC (PD-L1 / all comers)	Cohort A fully recruited 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		

Portfolio of selective AXL inhibitors in clinical development



(1): Clinical trial collaboration with Merck & Co, no preferential rights (2) Investigator initiated trial programme, BerGenBio does not act a regulatory sponsor

Clinical development focus: Leukaemia & Lung Cancer



Bemcentinib monotherapy in R/R AML: 43% ORR*

Bemcentinib + LDAC: 46% ORR

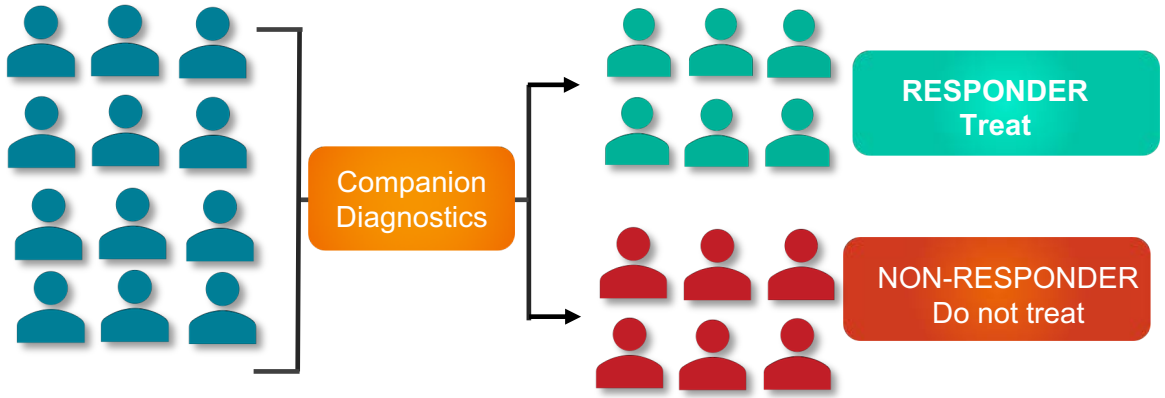
Bemcentinib combination with KEYTRUDA in 2L NSCLC: ORR* 40% and mOS 12.2months.

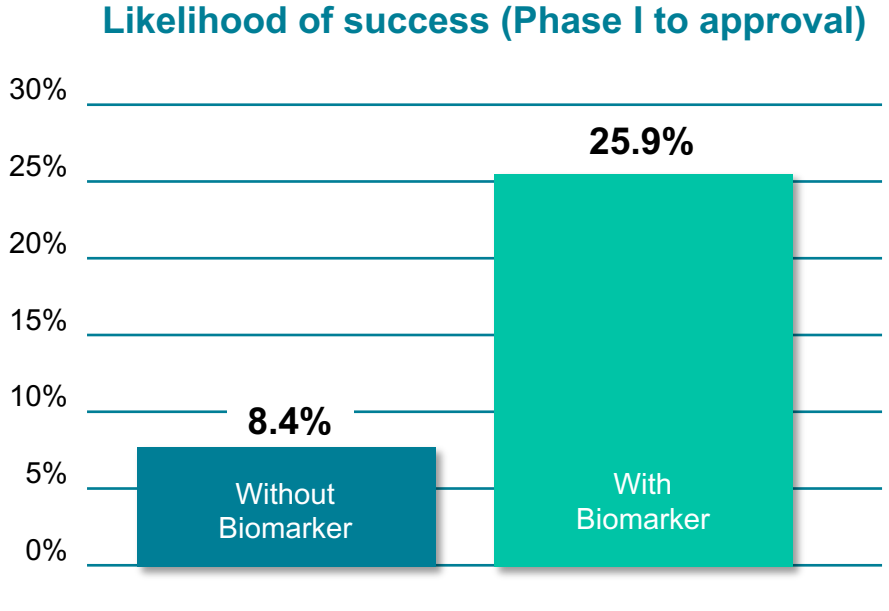
Additional indications with strong rationale and KOL endorsement are being pursued through active support of broad ILS programme

PFS = Progression Free Survival ORR= Overall Response rate * AXL +ve patients by BGB biomarker assay (ca.50% patients)

Companion Diagnostics Development Programme (CDx)

- ✓ Selects AXL positive patients
- ✓ Enriched clinical trials
- ✓ Improved chances of regulatory success
- ✓ Precision medicine approach to reimbursement





CDx Development Programme

Liquid Biopsy

- Soluble AXL (sAXL) - Predictive Biomarker for AML/MDS
- Relapsed/Refractory AML/MDS patients with lower plasma levels of sAXL have shown greater response to bemcentinib monotherapy

Tissue Biopsy

- AXL IHC - Predictive Biomarker for NSCLC
- NSCLC patients with elevated levels of AXL tissue expression have shown improved ORR and PFS when treated with bemcentinib + KEYTRUDA*

* independent of PDL1, BGBC008 trial in 2L, IO naive NSCLC, all comers

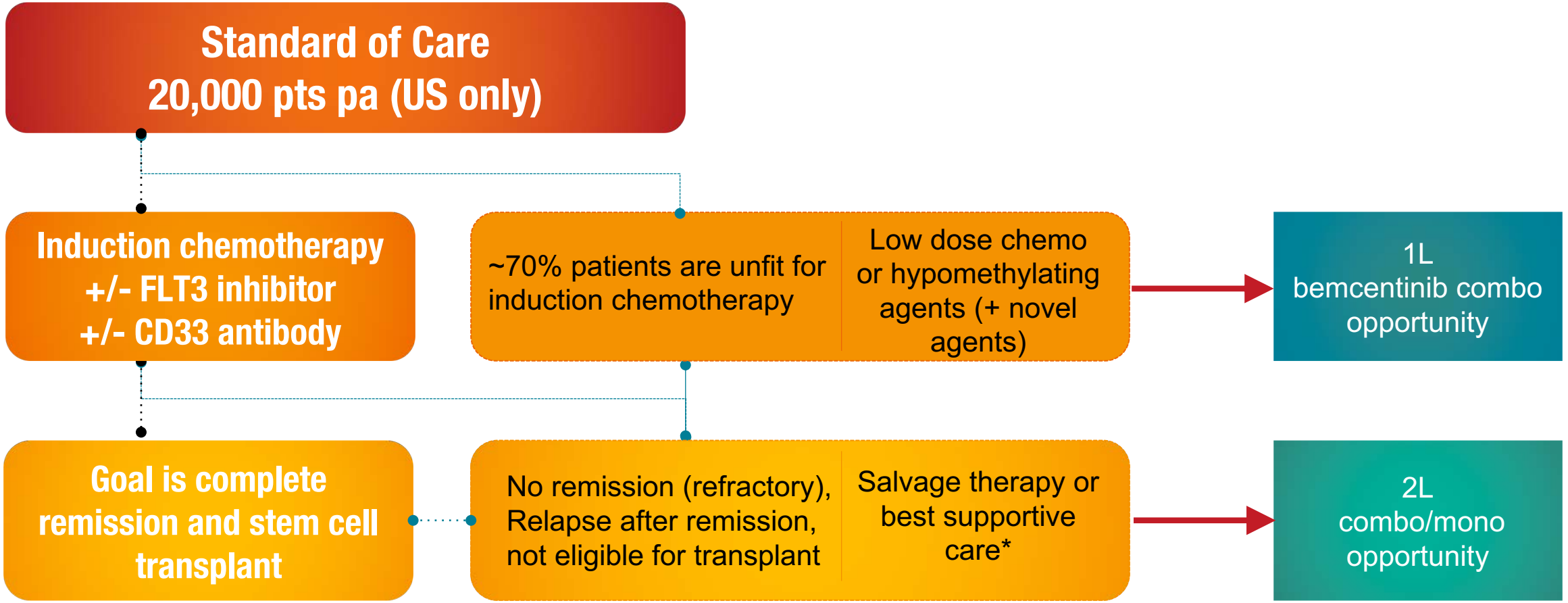
Ref. BGBC003 / NCT02488408

Acute Myeloid Leukaemia (AML)

Bemcentinib is being evaluated as a monotherapy and in combination with standard of care chemo therapy to treat AML

- ***Monotherapy 43% ORR in AXL +ve r/r AML***
- ***LDAC chemo combo 46% ORR in all comer r/r AML***

Acute myeloid leukemia (AML) is one of the most aggressive blood cancers, with a very low survival rate and few options for patients who are ineligible for intensive chemotherapy



MDS: Myelodysplastic syndrome, *a small fraction of patients may be eligible for targeted therapy

SOC & Recent Approvals in 1 Line AML treatment (all patients unsuitable for induction chemo)

SoC: HMA / Low dose chemo

- **HMA : decitabine / 5-azacytidine :** 26% ORR, 28% 1yr.survival, mOS 5.5 mo.
- **Low dose chemo: cytarabine (LDAC)** 2-18% ORR, mOS 4.9 - 8 mo.

Novel agent Combinations

- **BCL-2 inhibitor Venetoclax (Venclexta)** in combination with low dose chemo
  - 1L + decitabine: ORR 54%%, DoR 4.7mo. OR + azacitidine : ORR 37%. DoR 5.5 mo.
  - 2L + LDAC: ORR 21%, DoR 6mo.
- **1L: Hedgehog inhibitor Glasdegib (Daurismo)** in combination with LDAC
  - ORR 17%, mOS 8.3months.vs LDAC ORR 8-18%, mOS4.3 mo.

IDH Inhibitors (8-10% patients)

- **Ivosidenib (Tibsovo)** as monotherapy in IDH1-mutated patients: 30% ORR, DoR 8.2mo. mOS 8.8 mo.
- **Enasidenib (Idhifa)** as monotherapy in IDH2-mutated patients: 23% ORR, mDoR 8.2 mo, mOS 9.3 mo.

FLT3 Inhibitor (20% patients)

- **Gilteritinib (Xospata)** as a monotherapy in FLT3-mutated patients (ORR 21%)
- **Midostaurin (Rydapt)** in combination with standard cytarabine and daunorubicin therapy in FLT3-mutated patients: 23% reduction is risk of death.

HMA: Hypomethylating agent

The evolving 1L SOC in AML treatment

FDA U.S. FOOD & DRUG ADMINISTRATION

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FDA approves venetoclax in combination for AML in adults

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Drugs

Regulatory Science Research and Education

Development & Approval Process (Drugs)

Drug Safety and Availability

On November 21, 2018, the Food and Drug Administration granted accelerated approval to venetoclax (VENCLEXTA, AbbVie Inc. and Genentech Inc.) in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

Approval was based on two open-label non-randomized trials in patients with newly- diagnosed AML who were ≥ 75 years of age or had comorbidities that precluded the use of intensive induction chemotherapy. Efficacy was established based on the rate of complete remission (CR) and CR duration.

Content current as of: 12/14/2018

Regulated Product(s) Drugs

Study M14-358 (NCT02203773) was a non-randomized, open-label clinical trial of venetoclax in combination with azacitidine (n=67) or decitabine (n=13) in newly-diagnosed patients with AML. In combination with azacitidine, 25 patients achieved a CR (37%, 95% CI: 26, 50) with a median observed time in remission of 5.5 months (range: 0.4-30 months). In combination with decitabine, 7 patients achieved a CR (54%, 95% CI: 25, 81) with a median observed time in remission of 4.7 months (range: 1.0-18 months). The observed time in remission is the time from start of CR to data cut-off date or relapse from CR.

Study M14-387 (NCT02287233) was a non-randomized, open-label trial of venetoclax in combination with low-dose cytarabine (n=61) in newly-diagnosed patients with AML, including patients with previous exposure to a hypomethylating agent for an antecedent hematologic disorder. In combination with low-dose cytarabine, 13 patients achieved a CR (21%, 95% CI: 12, 34) with a median observed time in remission of 6 months (range: 0.03-25 months).

The most common adverse reactions (≥30%) to venetoclax in combination with azacitidine or decitabine or low-dose cytarabine were nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, fatigue, vomiting, peripheral edema, pneumonia, dyspnea, hemorrhage, anemia, rash, abdominal pain, sepsis, back pain, myalgia, dizziness, cough, oropharyngeal pain, pyrexia, and hypotension.

Summary:

Venetoclax in combination with HMA or low dose chemo

- 1L + decitabine: ORR 54%%, DoR 4.7mo. / + azacitidine : ORR 37%. DoR 5.5 mo.
- 2L + LDAC: ORR 21%, DoR 6mo.

Bemcentinib in combination with LDAC

- 1L/2L ORR 46%. DoR 6.2 mo. (immature), adverse event (>30%) diarrhea

Bemcentinib monotherapy

- >2L : AXL +ve patients ORR 43%, DoR 3.1mo.

Ref. BGBC003 / NCT02488408

Bemcentinib in AML

Monotherapy & in combination with low-dose chemotherapy

2L Monotherapy (completed)

2L and later-line R/R AML & MDS N = 36 pts

43%* CR/CRi/CRp in Axl +ve pts

* Ca. half of patients found to be AXL positive

Immune activation and clonal stabilisation observed

1L & 2L Combination Therapy (complete)

Decitabine combo
AML, N = 14 pts

Low-dose cytarabine (LDAC) combo
AML, N = 14 pts

ASCO 2019

46% ORR in LDAC combo AXL all comers

Endpoints

Primary
- safety / ORR

Secondary
- RFS
- OS
- biomarkers

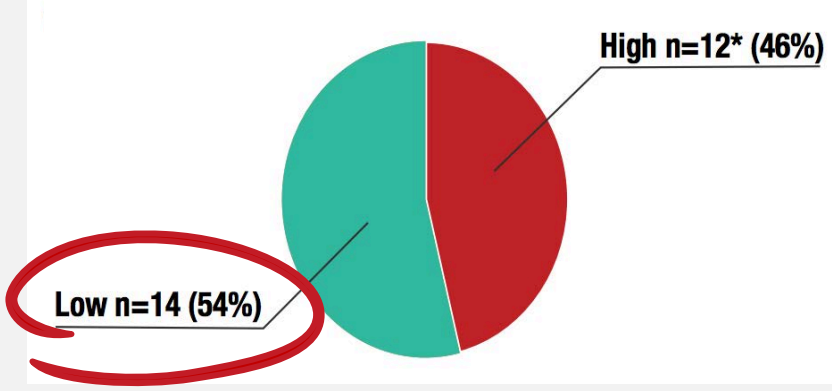
*LDCT: approved low dose chemotherapy regimens

Bemcentinib monotherapy exhibits potent anti-leukaemic activity 2L R/R patients

Biomarker:

Soluble AXL (sAXL) at screen:

Inversely correlated with AXL receptor activity



Superior response rate in patients positive for AXL biomarker

	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 3 cycles of treatment.*

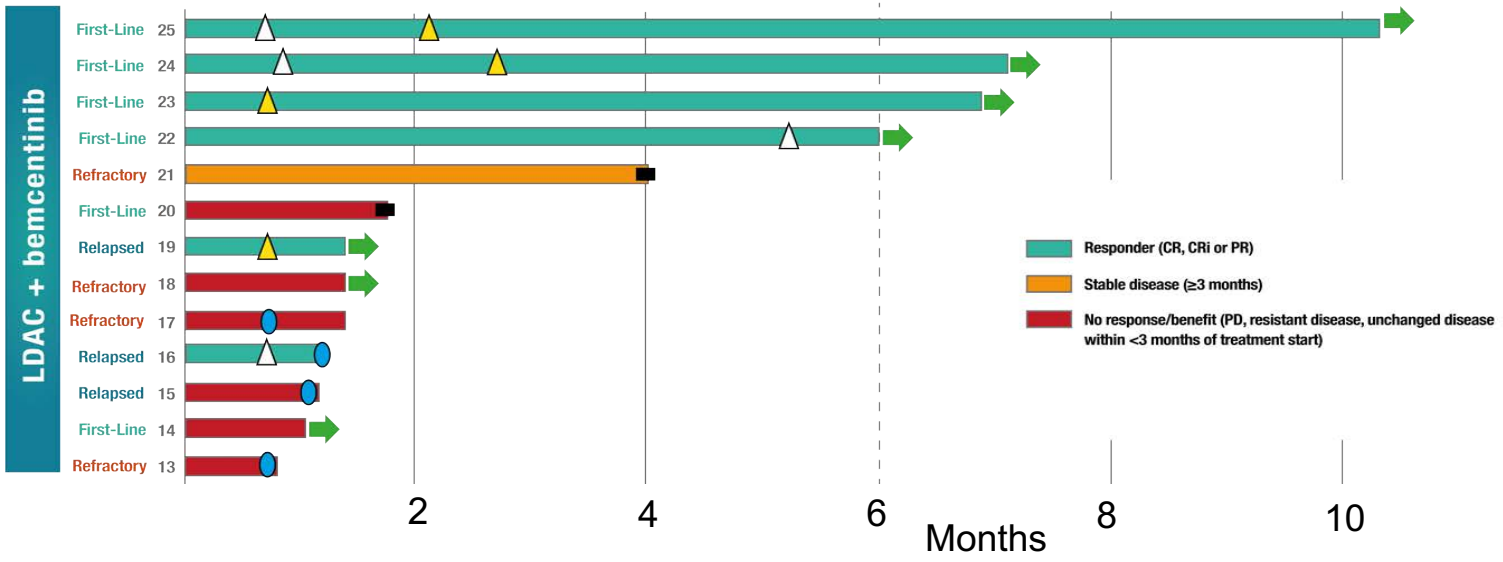
Median age of all patients: 74.5

Responses included poor risk and secondary disease

- ✓ **Bemcentinib monotherapy is well tolerated: mild and manageable side effect profile with low incidence of Grade 3/4 events**
- ✓ **Low incidence of hematological adverse effects**
- ✓ **mDoR 3.1mo. (5.5 mo. including 2 patients with low dose decitabine, one remains in CR after 20 months)**

Intention-to-treat population included 36 patients, 9 of whom were not evaluable for efficacy (8 were exposed to treatment for <21 days, 1 was a first line patient). sAXL levels were available for 25 evaluable patients.
Source: Loges, et al. ASH 2018.

Bemcentinib + LDAC combo exhibits potent and durable anti-leukaemic activity



Treatment Response History:

First-Line Patient has not been treated for AML prior to study

Relapsed Patient had response on most recent AML treatment regimen prior to study

Refractory Patient had no response to most recent AML treatment regimen prior to study

Responses in evaluable patients *

	n	CR/CRi	PR	CR/CRi rate (%)	ORR (%)
LDAC + bemcentinib	13	4	2	30.8%	46.2%

***Four responses** were observed in **first-line** patients.*
Four responses** were observed in patients with **secondary disease

Summary:

1L: 4/6 patients responded

2L Relapse: 2/3 patients responded

2L Refractory: 0/4 patients responded

LDAC + bemcentinib
Preliminary efficacy results

ORR: 46% (6/13)

6 responses have been reported (4 CR/CRi + 2 PR)

1 durable stable disease (≥3 months)

Current relapse-free survival in CR/CRi patients: 6.2 months (range: 0.7 - 9.6 months)

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Safety

Adverse Events

LDAC + bemcentinib		
AEs in ≥15% of patients	**Any grade**	**Grades ≥3**
Any event, n (%)	13 (81%)	12 (75%)
Haematologic		
Anaemia	4 (25%)	4 (25%)
Neutropenia*	3 (19%)	3 (19%)
Thrombocytopenia	3 (19%)	3 (19%)
Non-haematologic		
Diarrhoea	7 (44%)	1 (6%)
Dyspnoea	3 (19%)	1 (6%)
Electrocardiogram QT prolonged	3 (19%)	2 (13%)
Epistaxis	3 (19%)	0
Mouth haemorrhage	3 (19%)	0
Oedema peripheral	3 (19%)	0

- **Favourable safety profile cf. other LDAC combinations approved for AML**
- **Treatment-related adverse events were generally considered to be less problematic than for other TKIs**
- **Patients did not discontinue treatment for adverse events**

Deaths, Infections & Neutropenia

		LDAC + bemcentinib (n =16)
Early deaths	Death ≤30 days after treatment start	1 (6%)
	Death ≤60 days after treatment start	2 (13%)
Infections	Any serious infection reported**	2 (13%), 3 events
	Fatal infection within 60 days of starting treatment	1 (6%)
Neutropenia*	Incidence of neutropenia (number of pts)	3 (19%)
	Incidence of prolonged neutropenia, ≥10 days	1 (6%)

* Preferred terms included: neutropenia, febrile neutropenia

** Patients affected by any SAE falling under System Organ Class "Infections and infestations" (preferred terms included: Atypical pneumonia, Sepsis, Device-related infection, Urinary tract infection enterococcal, Pseudomonas infection, Escherichia sepsis)

Summary:

Venetoclax in combination with low dose chemo

- 1L + decitabine: ORR 54%%, DoR 4.7mo. / + azacitidine : ORR 37%. DoR 5.5 mo.
- 2L + LDAC: ORR 21%, DoR 6mo.

Bemcentinib in combination with LDAC

- 1L/2L ORR 46%. DoR 6.2 mo. (immature), adverse event (>30%) diarrhea

Bemcentinib monotherapy

- >2L : AXL +ve patients ORR 43%, DoR 3.1mo.

Conclusions

- Bemcentinib is well tolerated as monotherapy in >2L patients, offering meaningful duration of response in AXL +ve patients.
- The LDAC+bemcentinib combination showed promising efficacy among elderly AML patient population with 80% >75 years both as first-line in untreated newly diagnosed AML patients and as 2nd -5th line in relapsed AML patients
- Bemcentinib appears relatively safe and well tolerated in combination with both LDAC and cytarabine
- The ORR, seen in combination with LDAC, is higher than previously observed/historical benchmarks in single-agent cytarabine

Clinical Development in AML

1. First to market : ≥2L in elderly relapse AML : Bemcentinib monotherapy

- No approved SOC for elderly (>75yrs) relapse AML patients, only treatment option is supportive palliative care
- Patient population is ca. 50% AXL +ve by BGB sAXL biomarker
- 43% ORR with mDoR 3.1mo (5.5mo)*
  - * including 2 patients with low dose decitabine, one remains in CR after 20 months
- Very well tolerated, no immune suppression

Clinical development strategy: All comer phase IIb to be initiated H2'19 > Interim Analysis > Registration cohort
Potential for breakthrough and accelerated approval – FDA phase II meeting planned

2. Bemcentinib + LDAC : 1/2L relapse elderly AML

- Bemcentinib + LDAC appears well tolerated when compared to other LDAC combinations
- The ORR, observed in mixed line patient population is encouraging relative to other LDAC combinations and significantly higher than previously observed/historical benchmarks as single-agent.
- ORR of 46% was reported in an all-comer AXL patient population, with mDoR exceeding that of other LDAC combinations, whilst still not mature.
- Best response (6/9 patients) observed in 1L & 2L relapse patients

Clinical development strategy: All-comer expansion of current phase IIa trial, to be initiated H2'19.

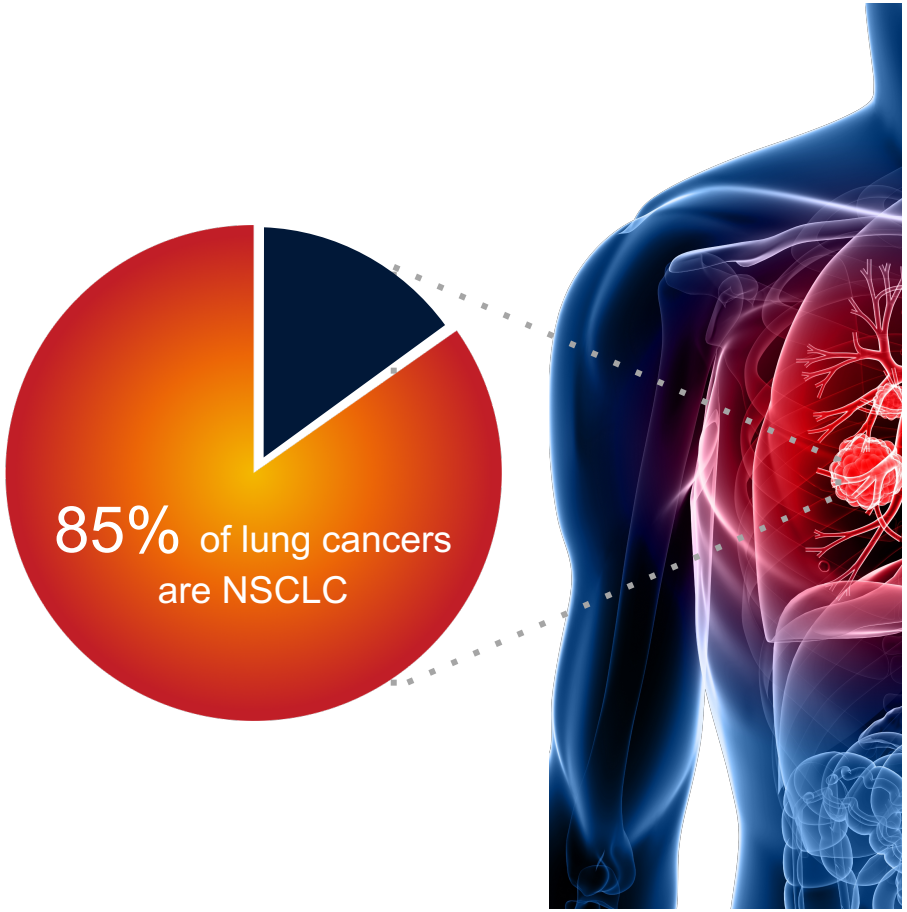
Ref. BGBC008 / NCT03184571

Bemcentinib in NSCLC: Combination with anti-PD(L)1

PoC data in combo with KEYTRUDA, previously treated, Chemo & IO relapse NSCLC patients*:*

- ***27% ORR in PD-L1 –ve patients***
- ***40% ORR in AXL+ve patients***

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



The largest cancer killer, most patients depend on drug therapy

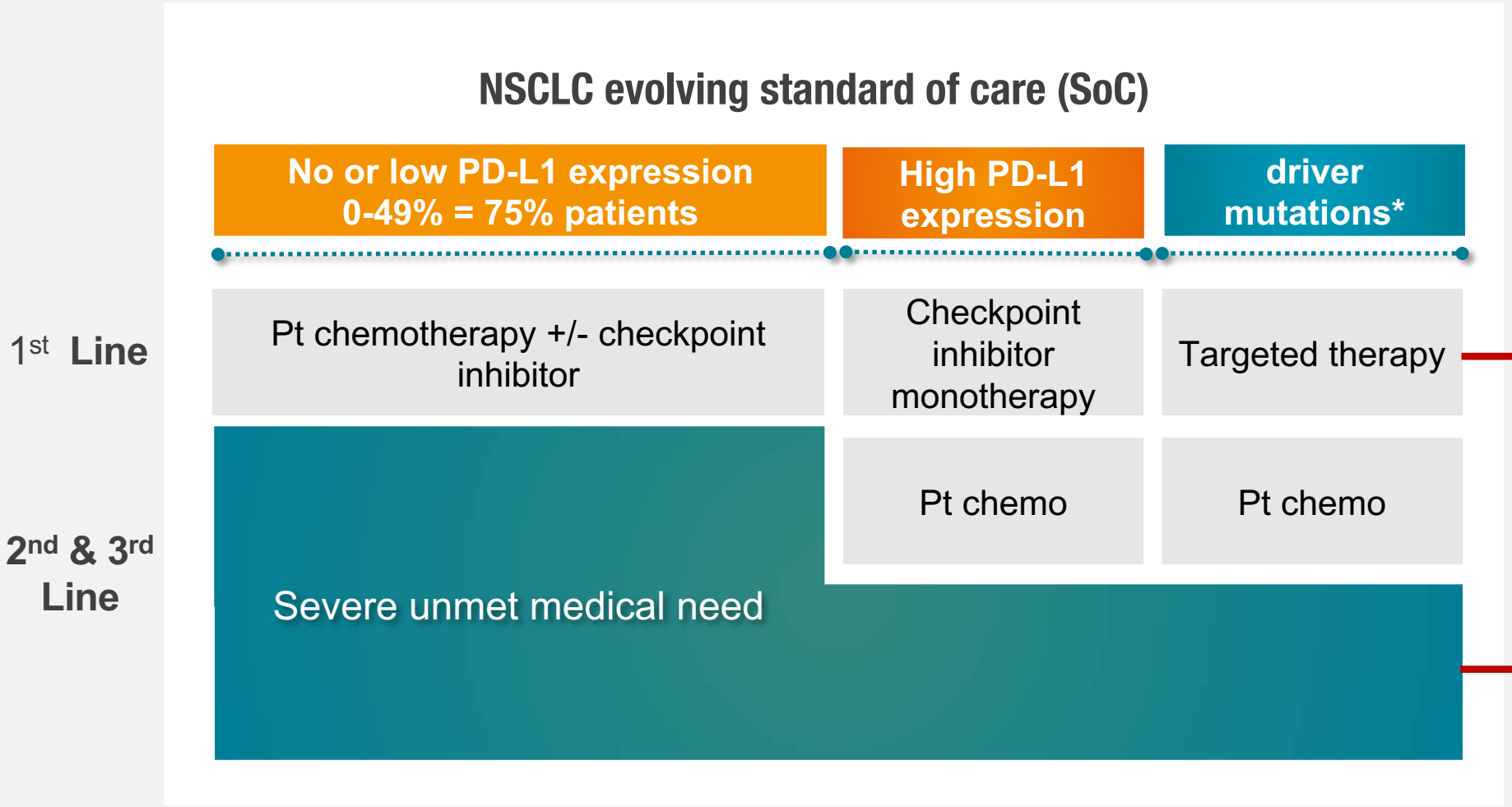
2.09 million new cases of lung cancer diagnosed/yr worldwide, making up 11.6% of all cancer cases[1]

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%[2]

(1) Globocan 2018 (2) Garon, E.B. et al. 5-Year Long-Term Overall Survival for Patients With Advanced NSCLC Treated With Pembrolizumab: Results from KEYNOTE-001. 2019 ASCO Annual Meeting.

Large unmet need in 2L NSCLC patients



Opportunity for bemcentinib

- **Deepening 1L responses, particularly PD-L1 negative/low**
- **Effective and well tolerated 2L therapies**

* Mutations / rearrangements with available targeted therapies such as EGFR and ALK

Comparison of: KEYTRUDA + bemcentinib (2L) vs KEYTRUDA + Chemotherapy (1L)

NSCLC 1L new SoC
KEYTRUDA + CT

PD-L1 0-49% 75% of patients*	ORR	mPFS	mOS (immature)	TEAE's ≥3
PD-L1 <1%	32%	6.1m	15m	67%
PD-L1 1-49%	48%	9m	NR	

NSCLC 2L, IO naïve, predominantly PD-L1 low
BGBC008: KEYTRUDA + bemcentinib

	ORR	mPFS (stage 1)	mOS (stage 1)	TEAEs ≥3
AXL +ve	40%	*5.9mo*	*12.2mo*	*17%*

2L Bemcentinib + Keytruda in AXL +ve / PD-L1 –ve/low patients revivals **1L** new SoC

* KN189

Opportunities to improve CPI efficacy in NSCLC

Pacheco et al. First Line IO ± Chemo in mNSCLC

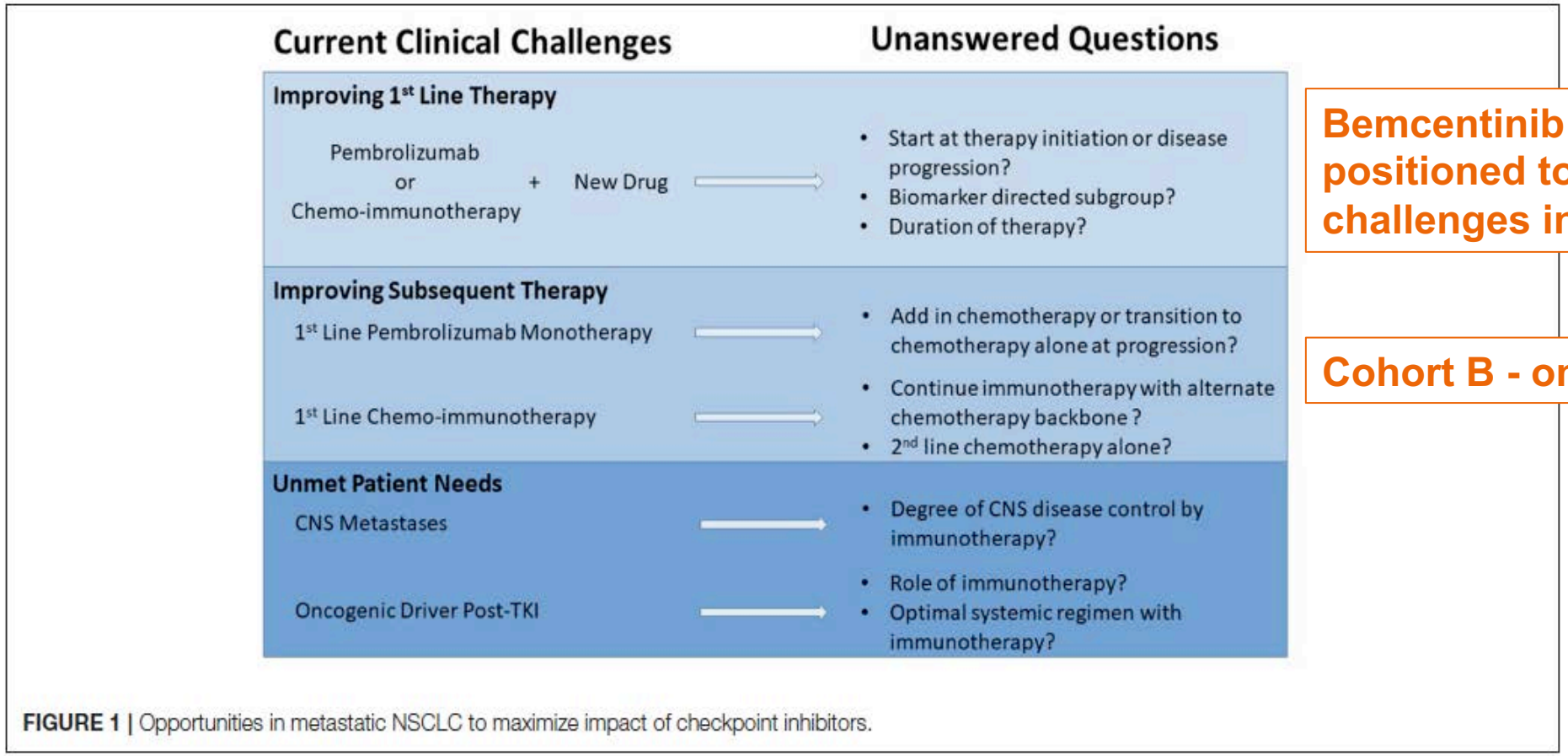


FIGURE 1 | Opportunities in metastatic NSCLC to maximize impact of checkpoint inhibitors.

Bemcentinib is ideally positioned to meet these challenges in 1L

Cohort B - ongoing

Frontiers in Oncology 2019, Jose Pacheco

BerGenBio

Bemcentinib + KEYTRUDA in 2L relapse NSCLC

Phase 2 Study Design

Cohort A
Previously treated, unresectable adenocarcinoma of the lung

PD-L1 / AXL all-comers

Chemo relapse (IO naïve)

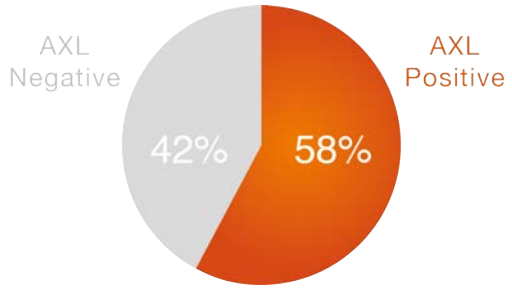
Cohort B

PD-L1 / AXL all-comers

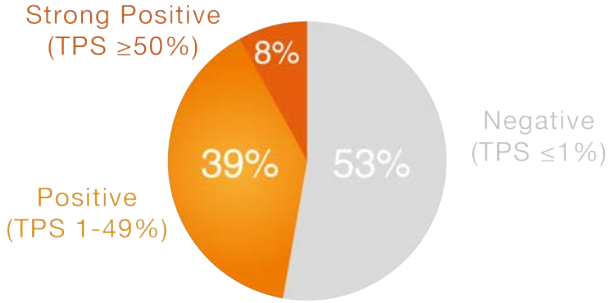
IO relapse

Stage 1		Stage 2
24 patients	If ≥ 4 PRs	24 patients
COMPLETE		COMPLETE
November 2018		ASCO 2019
Efficacy & mPFS presented: Society for Immunotherapy in Cancer (SITC)		Preliminary Data
N = 13 pts	If ≥ 1 PRs	N = 16 pts
RECRUITING		

AXL Status: n = 33
28 with at least 1 radiological assessment



PD-L1 Status: n = 38
29 with at least 1 radiological assessment

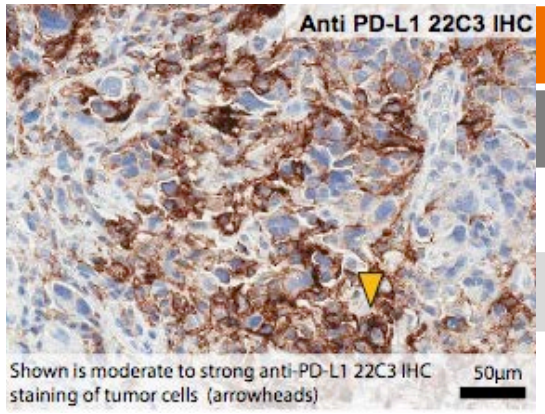


Key objectives

- Evaluate safety of the combination and response to treatment with the combination
- Characterise patients by PD-L1 and AXL status
- Evaluate efficacy of patients by biomarker status, and assess predictive qualities of biomarkers
- Assess survival measures in patients by biomarker status

Results: Predominantly PD-L1 low/negative patient population not expected to benefit from KEYTRUDA monotherapy

- Majority of patients not expected to benefit from KEYTRUDA monotherapy[1] based on their PD-L1 status
- Approx half of patients found to be AXL positive by IHC

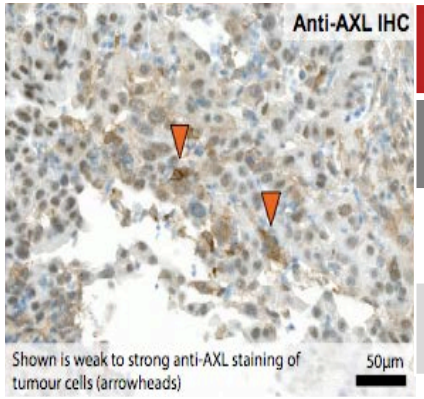


PD-L1 expression BGBC008

TPS (%)	<1	1-49	>50	total
n	20	15	3	38*
%	53	39	8	100
Historical ORR monotherapy [1]	9%	14%	47%	

* At time of data cut off evaluable for tumour PD-L1

(1) Garon *et al NEJM* (2015) Fig S4



AXL expression

Status	Neg	Pos.	total
n	14	19	33*
%	42	58	100

* At time of data cut off evaluable for tumour AXL

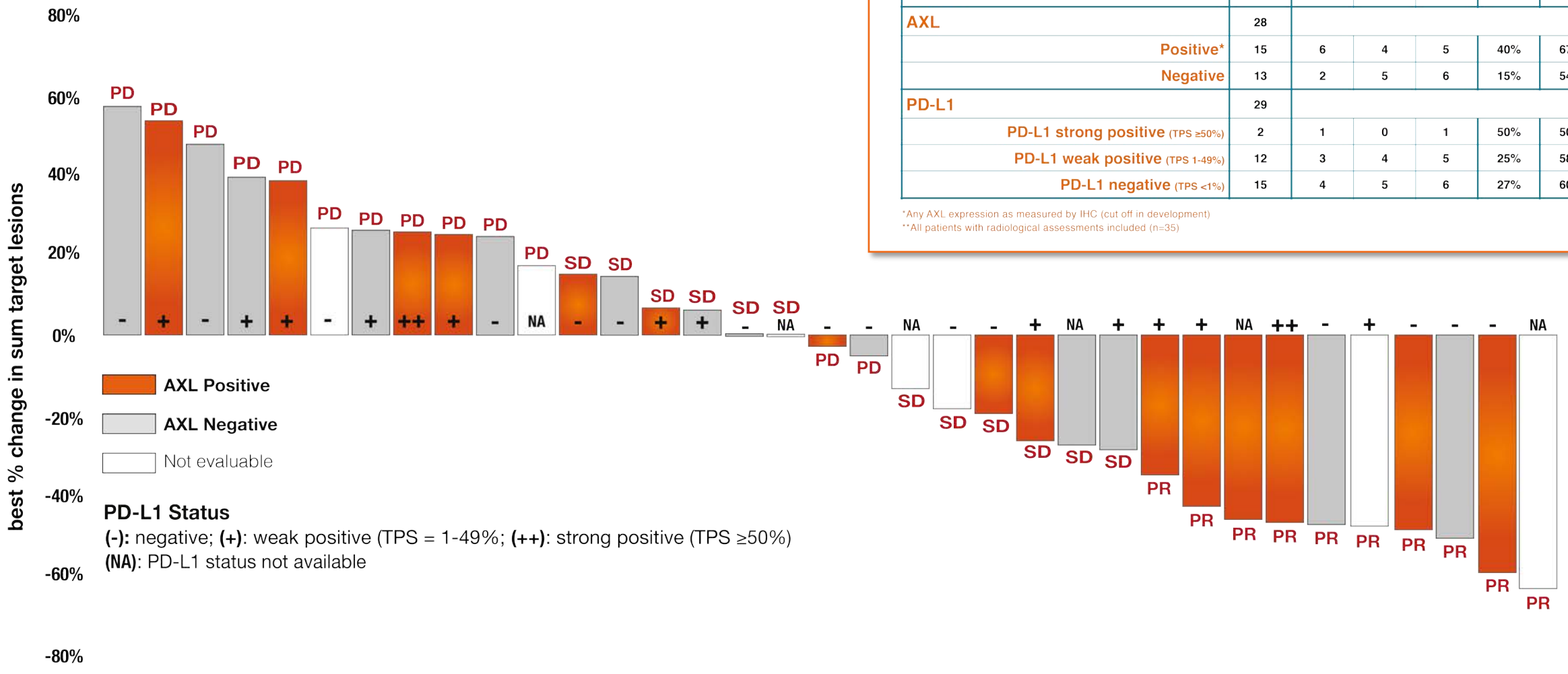
Krebs *et al* SITC 2018 (November 2018)

Antitumour activity* Change in tumour size from baseline (by AXL IHC)

40% ORR & 67% Clinical benefit in AXL+ve patients, irrespective of PD-L1 status.

	n	PR	SD	PD	ORR (%)	CBR (%)
Overall**	35	10	12	13	29%	63%
AXL	28					
Positive*	15	6	4	5	40%	67%
Negative	13	2	5	6	15%	54%
PD-L1	29					
PD-L1 strong positive (TPS ≥50%)	2	1	0	1	50%	50%
PD-L1 weak positive (TPS 1-49%)	12	3	4	5	25%	58%
PD-L1 negative (TPS <1%)	15	4	5	6	27%	60%

*Any AXL expression as measured by IHC (cut off in development)
**All patients with radiological assessments included (n=35)



* Preliminary data ASCO 2019

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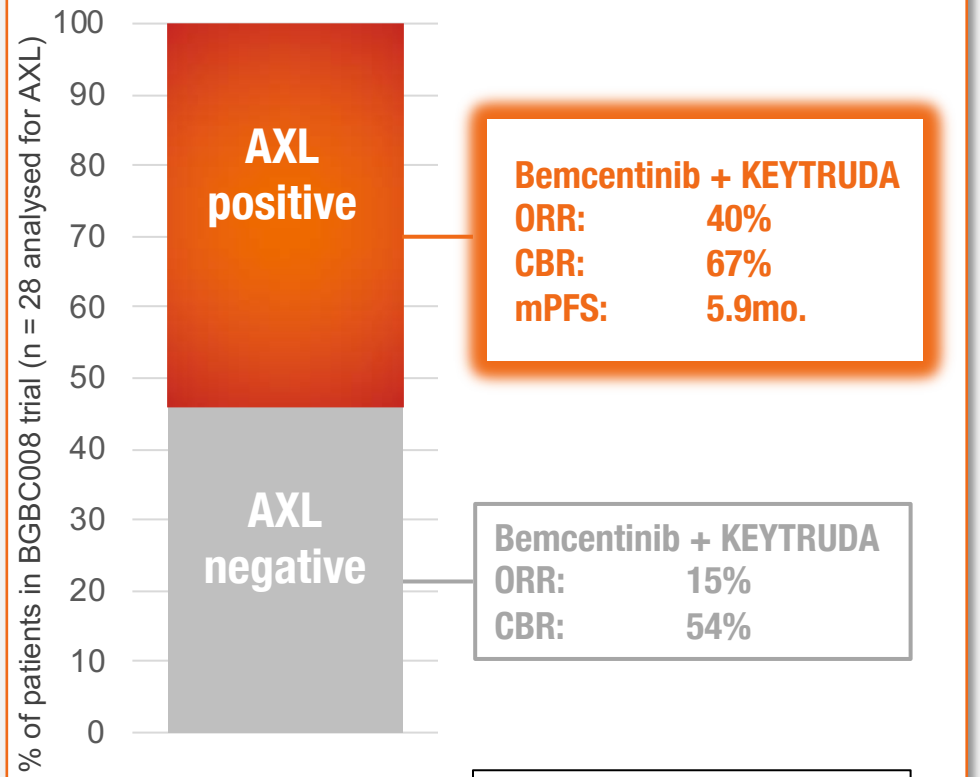
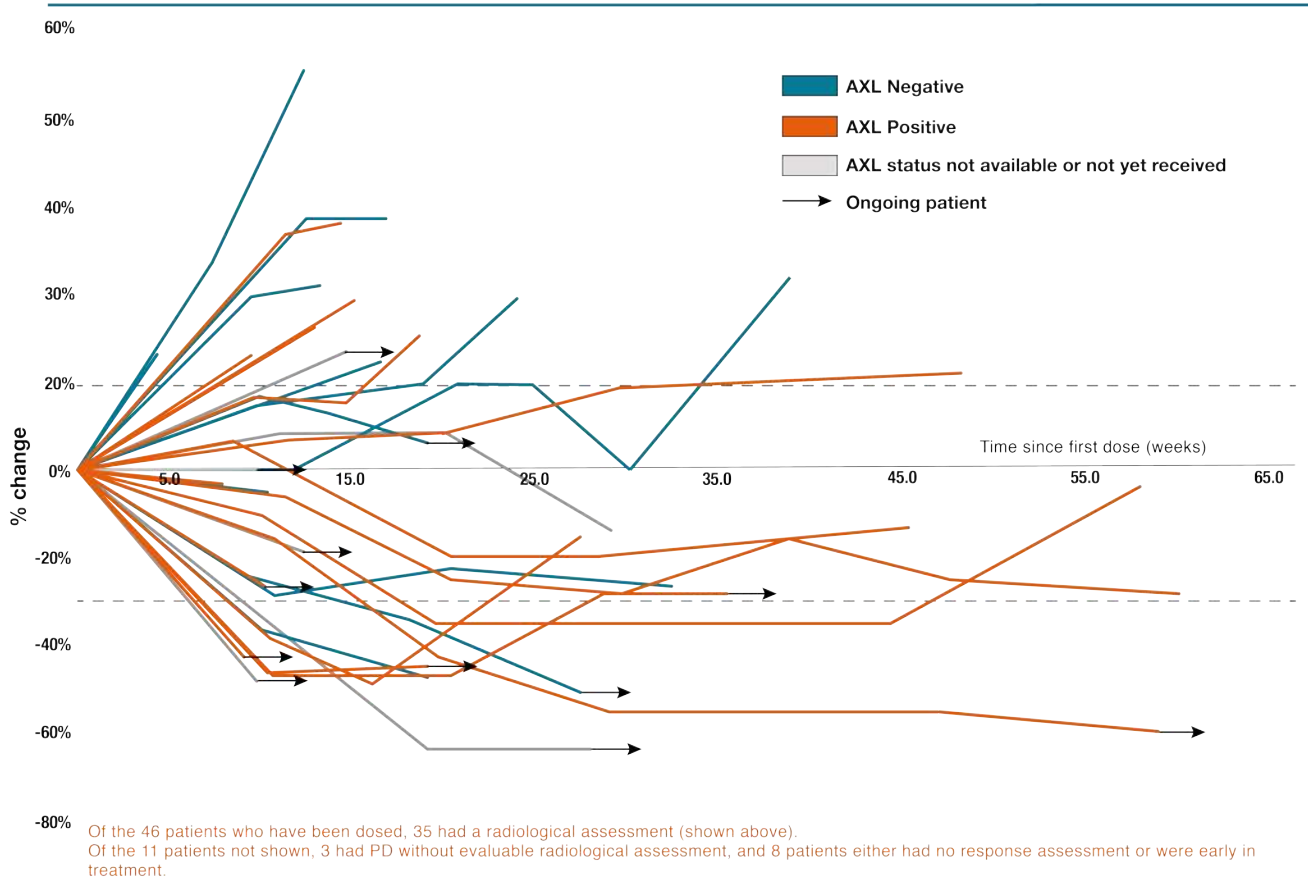
PoC data bemcentinib + KEYTRUDA: Superior efficacy in AXL +ve pts.





* PD-L1: 0 - 49%, Garon *et al* (2015), response rates between 8% (PDL1 negative) and 12-16% (PDL1 1-49%)

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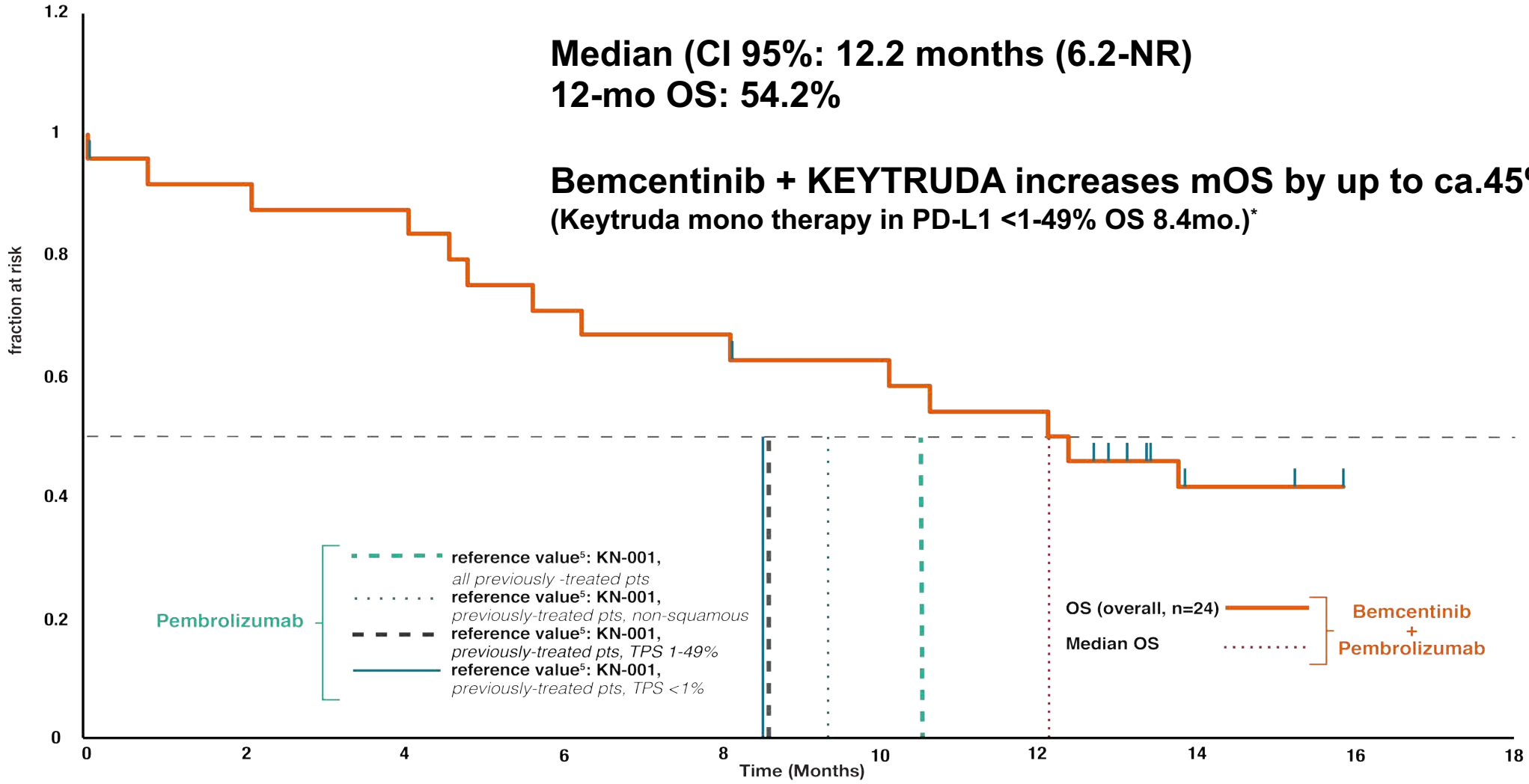
Median overall survival in stage I patients (n=24)



*Garon et al. KEYNOTE-001: Pembrolizumab for the Treatment of Non–Small-Cell Lung Cancer. NEJM, 2015.

Safety

- **The safety profile 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 problematic than for other TKIs or CPI combinations used in NSCLC**

Safety

Most frequent TRAEs (occurring in >10% of dosed patients)

n = 46

Preferred term	All grades		Grades ≥3	
	n	%	n	%
Transaminase increase*	16	35%	6	13%
Asthenia / Fatigue	14	30%	2	4%
Diarrhoea	12	26%	0	0%
Nausea	6	13%	0	0%
Anaemia	5	11%	1	2%
Decreased appetite	5	11%	0	0%

* Preferred terms include: Alanine aminotransferase increased, Aspartate aminotransferase increased and Transaminases increased. All events were reversible

No grade 5 TRAEs were reported.

Conclusions

- Promising clinical activity continues to be seen overall, particularly in patients with AXL positive tumours, including those with weak or no PD-L1 expression
- The median overall survival has surpassed what has been shown historically in 2nd line treatment with PD-1 inhibitor monotherapy
- The studied population was predominantly PD-L1 negative (53%) patients who are less likely to benefit from pembrolizumab monotherapy treatment
- The studied population was predominantly AXL positive (58%) patients
- The combination of bemcentinib and pembrolizumab was well-tolerated.

Clinical Development in NSCLC

Step 1. 2L CPI relapse

- Emerging 1L combination of keyruda+CT has left a vacuum in 2L
- Keytruda+CT 1L PDL-1 0-49% ORR 32-49% with mPFS of 6 - 9 mo.
- 2L SoC is limited to docetaxel or clinical trial
- CPI 'salvage' represents a substantial unmet medical need

Clinical strategy: On-going cohort B IO relapse patients.
Potential for breakthrough and accelerated approval

BerGenBio

BGB149

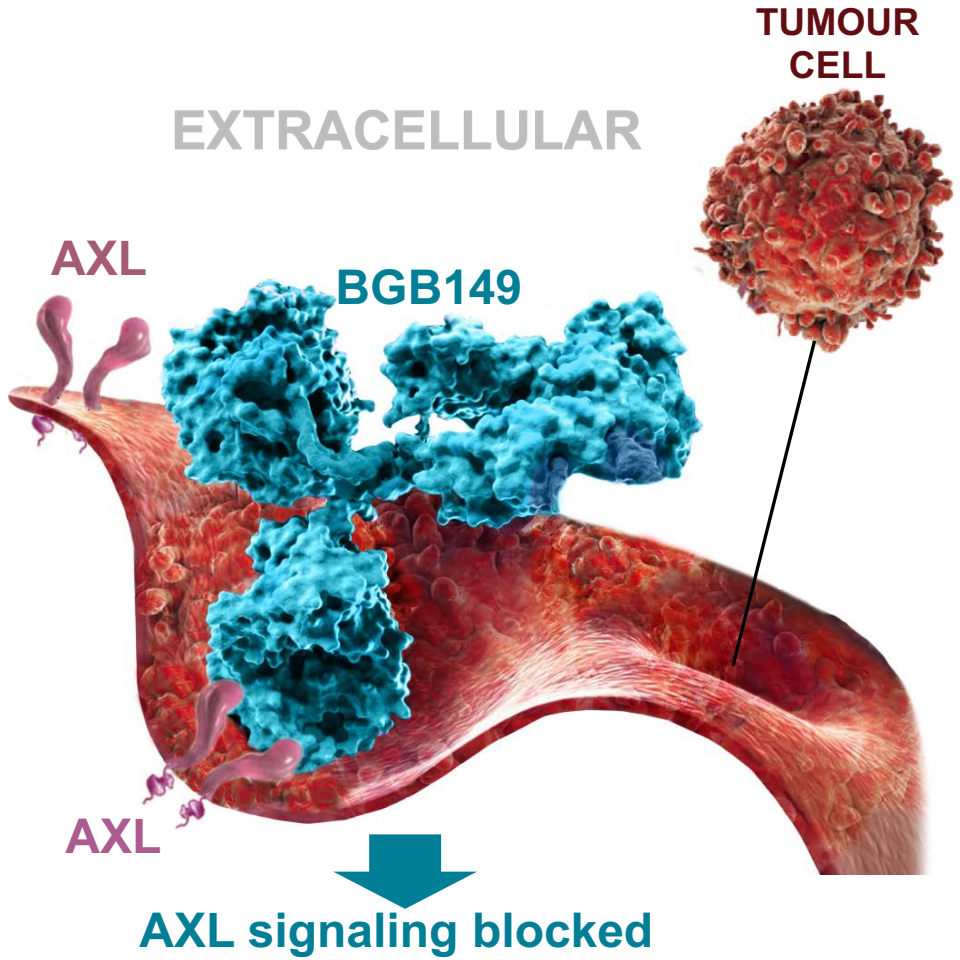
anti-AXL monoclonal antibody

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
- First-in-human healthy volunteer Phase I study initiated Up to 36 subjects, Safety, PK/PD
- First-in-patient trial expected in H2 2019



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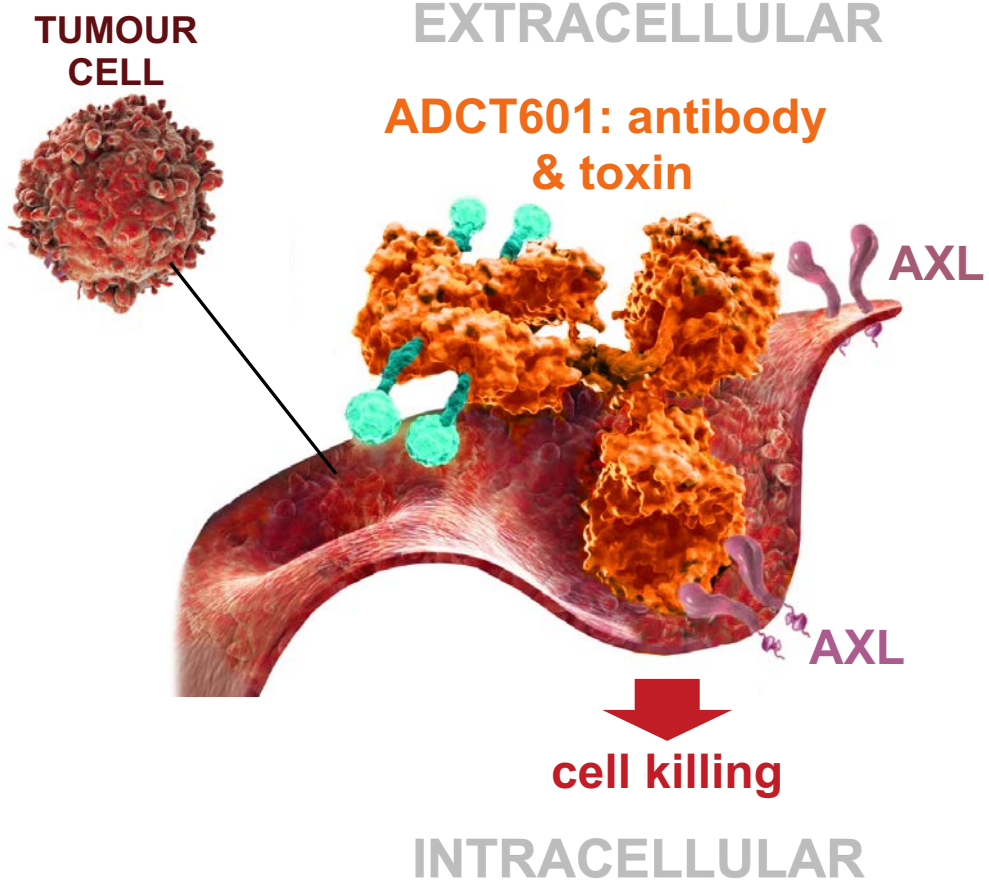
ADCT-601 – AXL ADC

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]

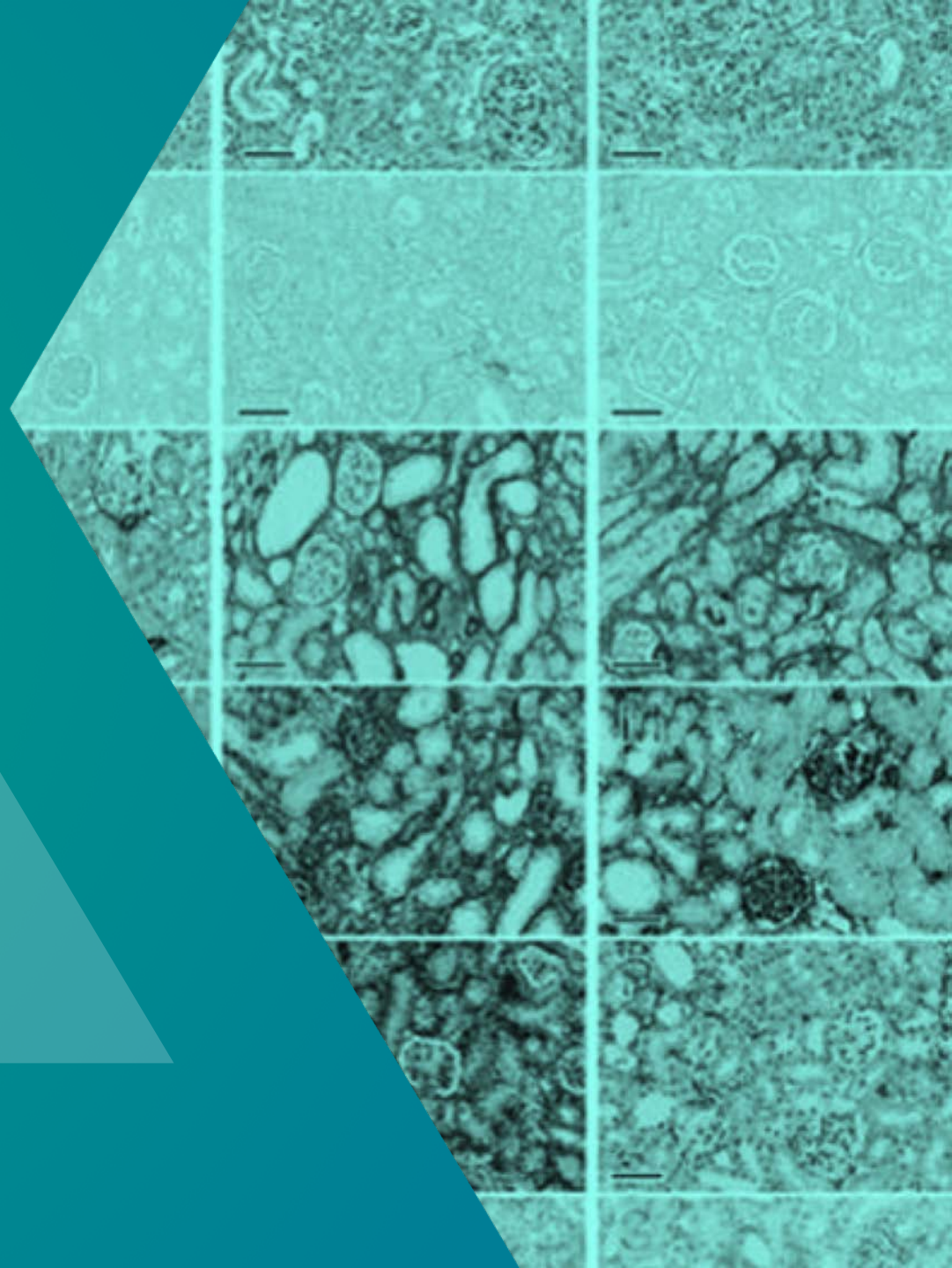
First-in-human Phase I study initiated in Jan 2019
- Solid tumours
- Up to 75 patients
- Safety, PK/PD, preliminary efficacy

Based on anti-AXL antibody BGB601 licensed from BerGenBio

(1) AACR 2018

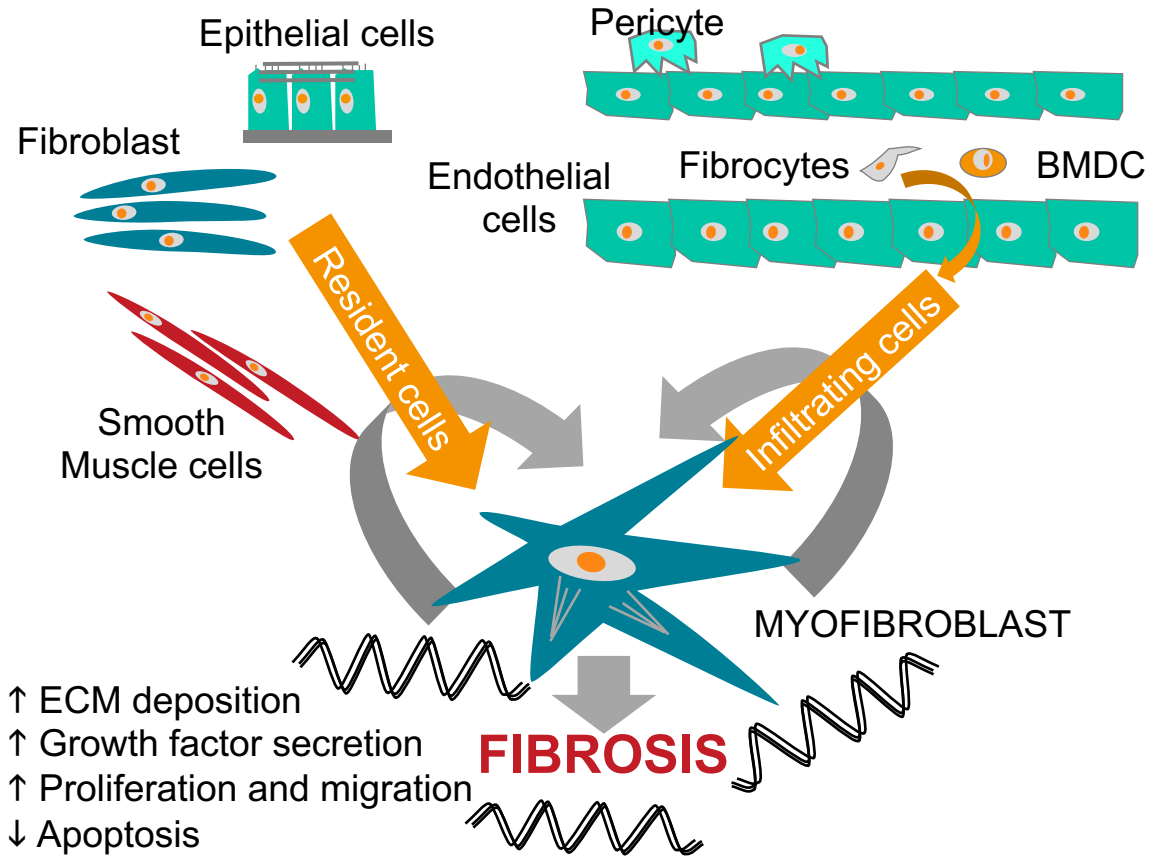
Fibrosis

- Fibrosis is the formation of excess fibrous connective tissue in an organ or tissue
- Physiologically, this can interfere with or totally inhibit the normal architecture and function of the underlying organ or tissue



The role of AXL in Fibrosis

Cells contributing to the development of fibrosis[1]



AXL

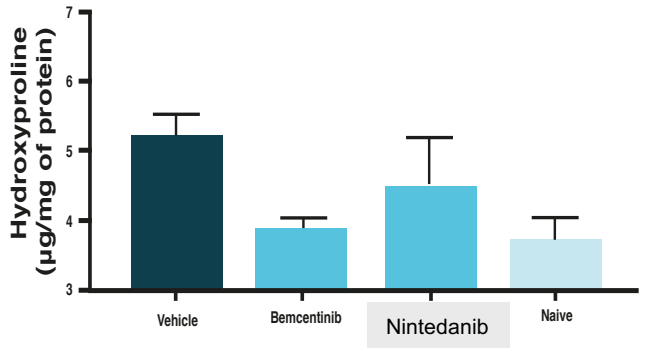
- Regulates and modulates key fibrogenic pathways
  - TGFβ signaling[2]
  - Mechanosensing Hippo pathway[3]
  - Peroxisome proliferator-activated receptor[4]
- Axl regulates cellular plasticity implicated in fibrotic pathologies e.g. EMT, EndMT, Macrophage polarity
- Axl elevated in keloid fibroblasts and modulates TGFβ[1] transcription[5]
- Axl required for hepatic stellate cell (HSC) activation[5]
- sAxl required for HSC ECM expression[5]
- Pharmacological modulation of Axl inhibits pre-clinical development of Liver (CCl4/Diet), Renal (UUO), Pulmonary (Asthma, Bleo) fibrosis

1 Gilbane ART 2015; 2 Reichl Hep. 2015; 3 Gibault ChemMed 2017; 4 Zhu AJTR 2016; 5 Barcena J. Hep 2015

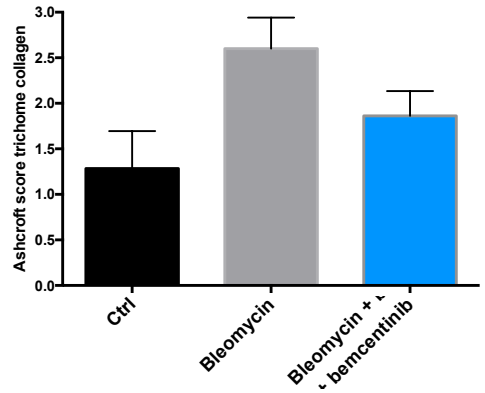
AXL inhibition prevents fibrosis in a panel of pre-clincial models

Lung

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

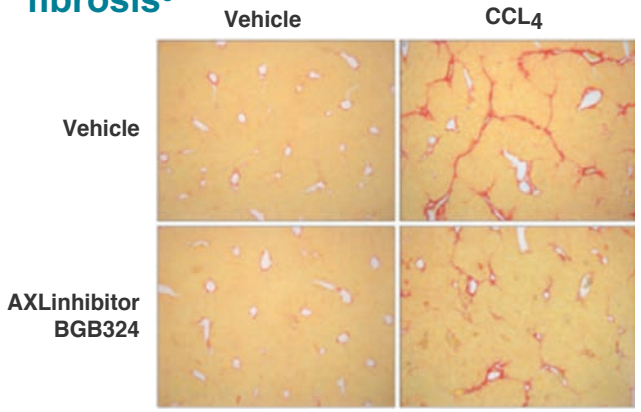


Bemcentinib reduces bleomycin induced fibrosis[2]

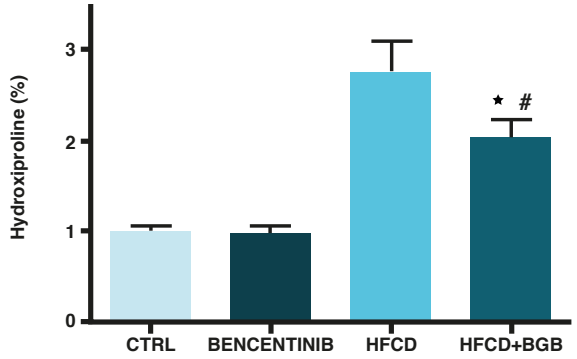


Liver

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



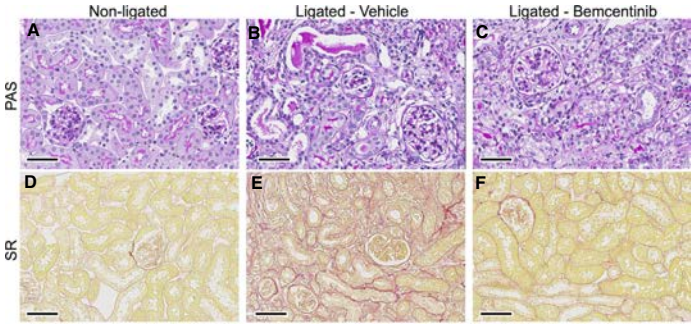
Bemcentinib reduces fibrosis in a diet induced model of NASH[4]



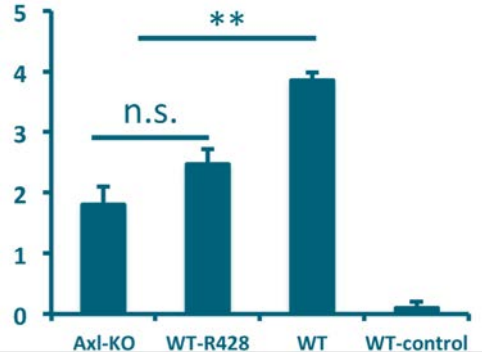
HFCD = high-fat, choline deficient diet
Leads to NASH in animal models

Kidney

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



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

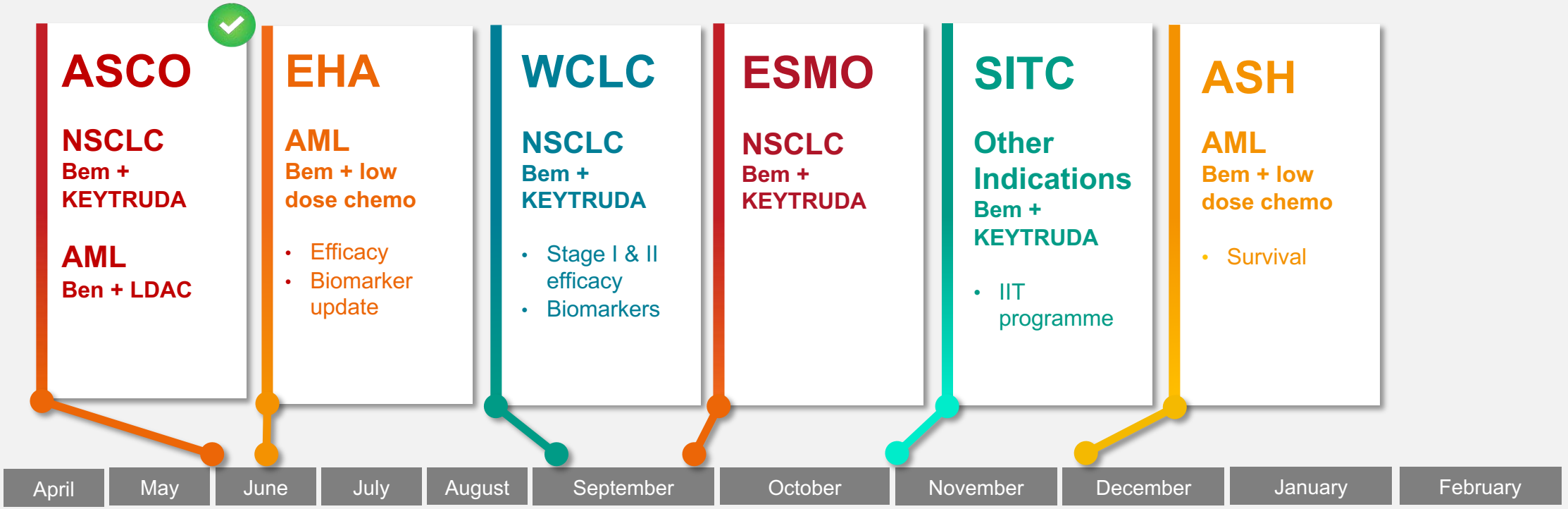


1 Espindola et al., 2018; 2 BerGenBio ASA; 3 Barcena et al., 2015; 4 Tutsaus et al., unpublished; 5 Landolt et al., 2019 6 Zhen et al., 2018

Competitive Landscape

AXL inhibitors - competitive landscape

Newsflow
H2, 2019



ASCO-SITC: Clinical Immuno-Oncology symposium, San Francisco
ASCO: American Society of Clinical Oncology, Chicago
WCLC: World Conference of Lung Cancer, Toronto
ESMO: European Society of Medical Oncology, Munich

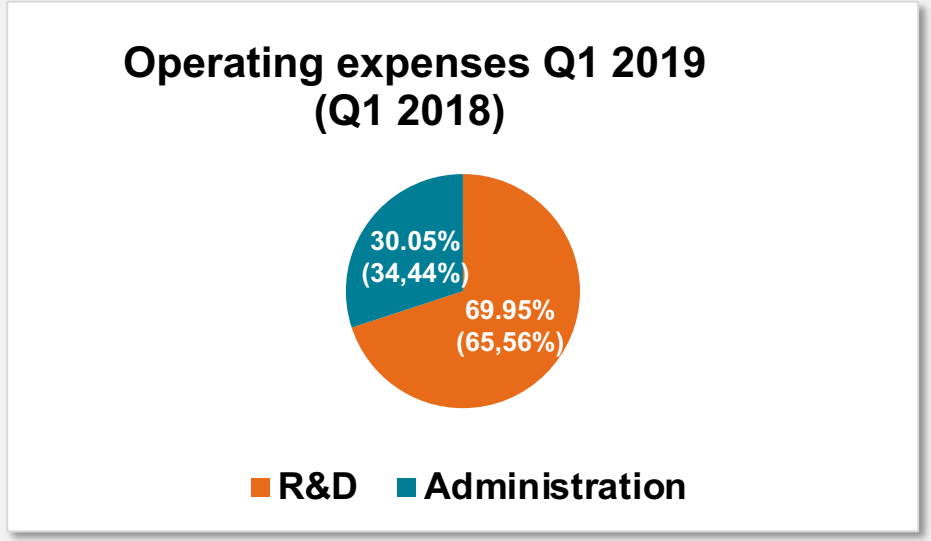
AACR: American Association for Cancer Research, Chicago
EHA: European Hematology Association, Stockholm
SITC: Society for Immunotherapy of Cancer, DC
ASH: American Society for Hematology, San Diego

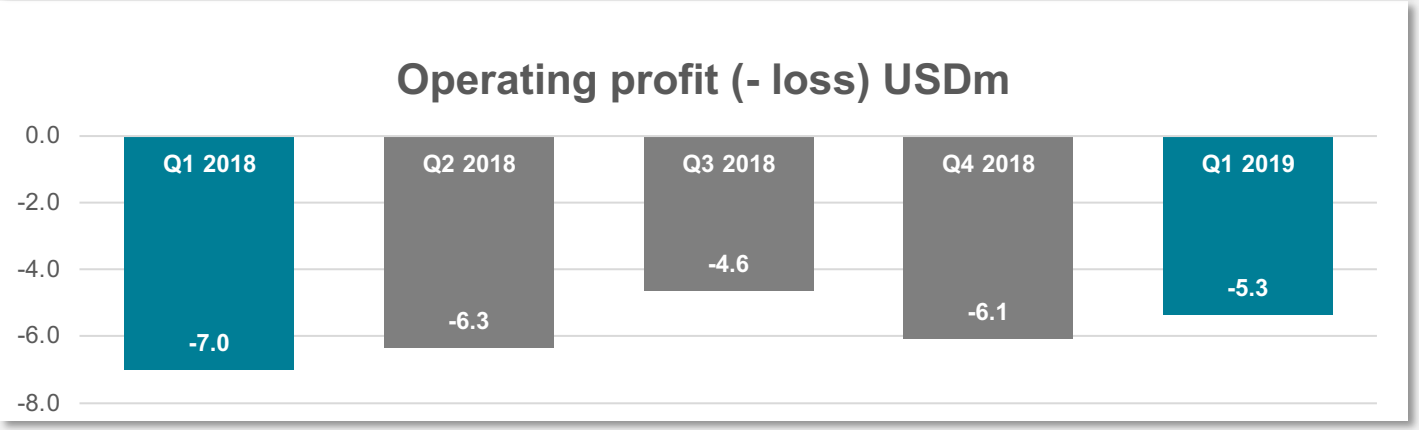
BerGenBio

Financials Q1 2019

Key financial figures Q1 2019

(USD million)	Q1 2019	Q1 2018	FY 2018
Operating revenues	1.0	0	0,3
Operating expenses	6.3	7.0	24.2
Operating profit (-loss)	-5,3	-7.0	-23.9
Profit (-loss) after tax	-5,2	-6.9	-23.6
Basic and diluted earnings (loss) per share (USD)	-0,09	-0,14	-0.44
Net cash flow in the period	-6.3	-5.2	-1.2
Cash position end of period	35.7	42.3	41.5



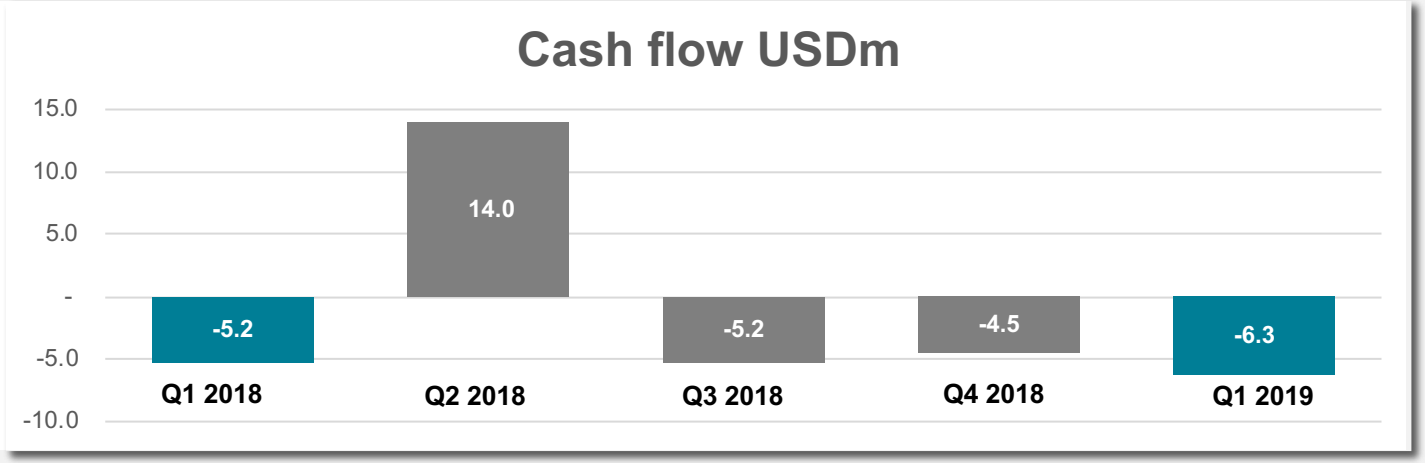


- Effective organisation
- 69.95% of operating expenses in Q1 2019 (Q1 2018: 65,56%) attributable to Research & Development activities

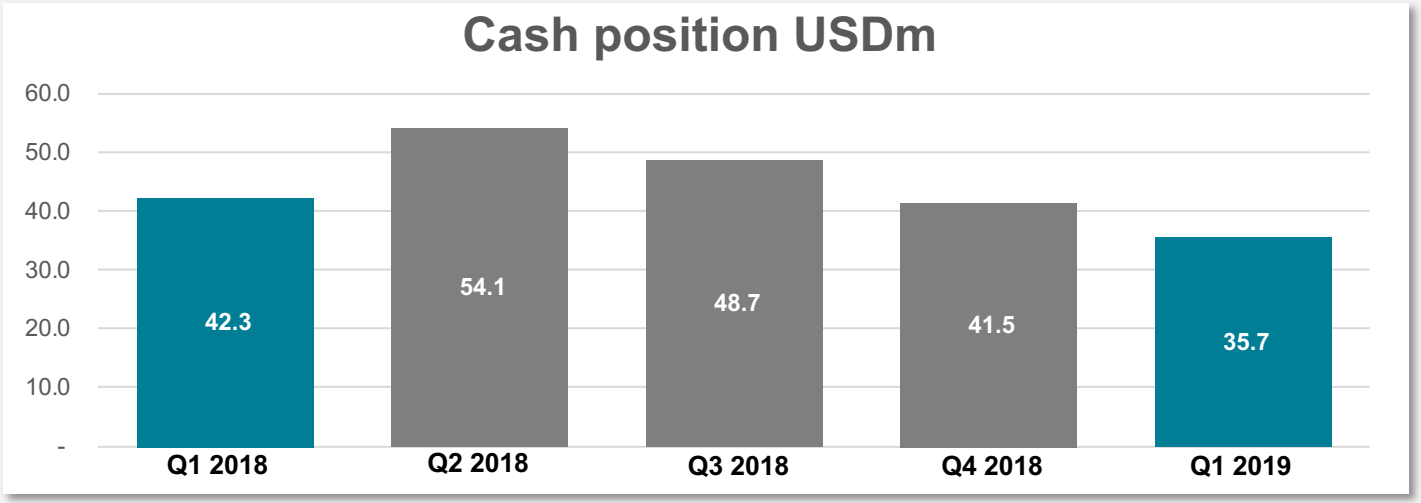
- Revenue USD 1.0 million, clinical milestone licence revenue received (ADCT-601)

http://www.bergenbio.com/investors/reports/quarterly-reports/

Cash flow and cash position



- Private placement Q2 18 strengthened cash position - gross funds raised USD 24 million (NOK 187 million)
- Quarterly cash burn average (Q118 – Q119) USD 5.9 million (NOK 48.4 million)



- Cash position Q1 2019 USD 35.7 million (NOK 306.7 million) - gives runway to deliver key clinical read outs from ongoing clinical studies
- Cash runway into 2020 based on current burn rate

Analyst coverage

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Appendix

BerGenBio

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 canbe 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

Fibrosis

Hogaboam, C.,*et al.,*(2017) 'Evaluation of TAM receptors inhibitors in IPF,' Keystone Symposium.

- 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).

Staufer K.,*et al.,*(2017) 'The non-invasive serum biomarker soluble Axl accurately detectsadvanced 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 targetingreduces fibrosis via hepatic stellate cell inactivation.*J Hepatology*

- Axl levels paralleled HSC activation
- Axl ko 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.

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