Phase II open-label, multi-centre study of bemcentinib (BGB324), a first-in-class selective AXL inhibitor, in combination with pembrolizumab in patients with advanced NSCLC.

abstract #: 3078

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Background & objective

NCT03184571: Phase II clinical trial of selective AXL inhibitor bemcentinib and pembrolizumab

Simon-like two stage design enrolling up to 48 patients

2nd line advanced adeno NSCLC
- IO naive
- Prior platinum doublet therapy
- measurable disease
- fresh tissue biopsy
- PDL1 all comers

Single arm
bemcentinib, 200mg daily
+
pembrolizumab, 200mg q3wks

Interim analysis

Final analysis

Key inclusion and exclusion criteria

- Histopathologically or cytologically documented Stage IV adenocarcinoma NSCLC
- Has disease progression on or after a prior platinum-containing chemotherapy
- Measurable disease as defined by RECIST 1.1
- Provision of suitable fresh tumour tissue for the analysis of AXL kinase and PD- L1 expression
- Eastern Cooperative Oncology Group (ECOG) performance score 0 or 1
- Not received more than one prior line of chemotherapy for advanced or metastatic adenocarcinoma of the lung
- No prior therapy with an immunomodulatory agent
- No symptomatic central nervous system (CNS) metastases and/or carcinomatous meningitis
- No recent or ongoing systemic steroid therapy

Assessments - efficacy & safety

- Response was assessed every 9 weeks per RECIST v1.1
- Adverse events were assessed by CTCAE v4.03
- Safety-evaluable: ≥1 dose of study treatment as of data cutoff 17 May 2018
- Recruitment into Part One has been completed

Biomarker analysis

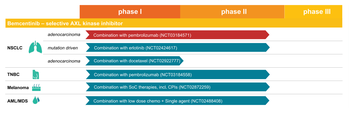
- PD-L1 and AXL expression per IHC
- Soluble protein biomarkers by liquid biopsy
- Immune cell popoulations by multi-spectral imaging

Endpoints

- **Primary**: ORR
- **Secondary**:
  DCR, DoR, PFS, Survival at 12 months, response by biomarker expression

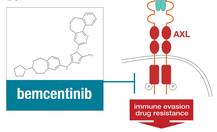
Bemcentinib (BGB324): selective, oral small molecule inhibtor of AXL in phase II clinical testing

Bemcentinib is developed in combination with immune-, targeted and chemotherapy in NSCLC, AML/MDS, melanoma and TNBC.



Selectivity Profile

Kinase	Kinome Scan (Kd)	
	nM	Fold
Axl	0.4	1
Mer	100	250
Tyro	>1000	>1000



Study rationale

anti PD-1 therapies in second line metastatic non-small cell lung cancer (NSCLC)

- Pembrolizumab as a single agent is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-containing chemotherapy and whose tumors express ≥1% PD-L1
- In a randomised phase II/III trial of pembrolizumab vs docetaxel for previously treated, PD-L1-positive, advanced NSCLC (KEYNOTE-010, Herbst et al) pembrolizumab was found to
  - prolong OS in patients with PD-L1 ≥1%
  - prolong PFS in pts with PD-L1 ≥50%
  - 1 year survival was 18% and 30% in patients with ≥1% and ≥50% PD-L1, respectively
- Novel combination treatment strategies are needed to improve efficacy of pembrolizumab

AXL receptor tyrosine kinase and selective AXL inhibitor bemcentinib

- AXL is a receptor tyrosine kinase expressed on tumour and immune cells and a member of the TAM family (Tyro-AXL-Mer) of kinases
- AXL is overexpressed in response to a hostile tumour microenvironment and drives a tumour survival programme:
  - AXL drives immune escape
  - anti-tumour therapy resistance
  - metastasis
- AXL is a negative prognostic factor in a multitude of cancers including NSCLC

- Bemcentinib, a first-in-class highly selective inhibitor of AXL, has been shown to improve the efficacy of checkpoint blockade in murine pre-clinical models of NSCLC by
  - improving anti tumour response when given in combination with immune checkpoint inhibitors compared to checkpoint inhibitors alone
  - supporting an anti-tumour cytokine profile
  - leading to increased tumour immune cell infiltration

First stage completed enrollment: Preliminary interim analysis of RECIST evaluable patients to date, study remains ongoing

Patients

Table 1: Baseline demographics

Age, median (range)	64 (51 - 77)
ECOG at screen, median (range)	1 (0 - 2)
0	6 (25%)
1	10 (41.7%)
2	8 (33.3%)
# previous treatments treatments, median (range)	1 (0 - 1)
Best response to most recent treatment, n (%)	
PR/CR	6 (25%)
SD	9 (37.5%)
PD	8 (33.3%)
Other/unknown	1 (4.2%)
Mutations, n (%)	
KRAS	3 (12.5%)
TP53 and ERBB2	1 (4.2%)
none	19 (79.2%)
Metastases, n (%)	
Liver	4 (18.2%)
bone	5 (22.7%)
adrenal	3 (13.6%)
CNS / Spinal	1 (4.5%)
pancreas	1 (4.5%)
kidney	1 (4.5%)

Safety

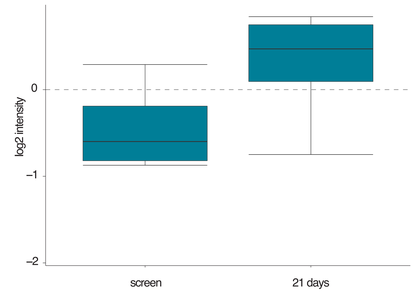
Table 2: Treatment emerging adverse events related to either bemcentinib, pembrolizumab or both

MedDRA system organ class	possibly related ≥ Grade 3
Blood and lymphatic system disorders	1
Gastrointestinal disorders	-
General disorders & administration site conditions	2
Hepatobiliary disorders	3
Investigations	8
Metabolism and nutrition disorders	-
Musculoskeletal and connective tissue disorders	1
Respiratory, thoracic and mediastinal disorders	-
Skin and subcutaneous tissue disorders	2
Total	**17**

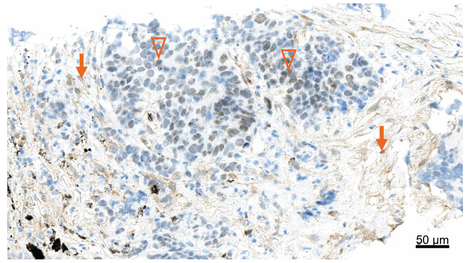
Adverse events are expressed as total number of events

Pharmacodynamics

Plasma soluble AXL levels increase upon treatment with bemcentinib + pembrolizumab



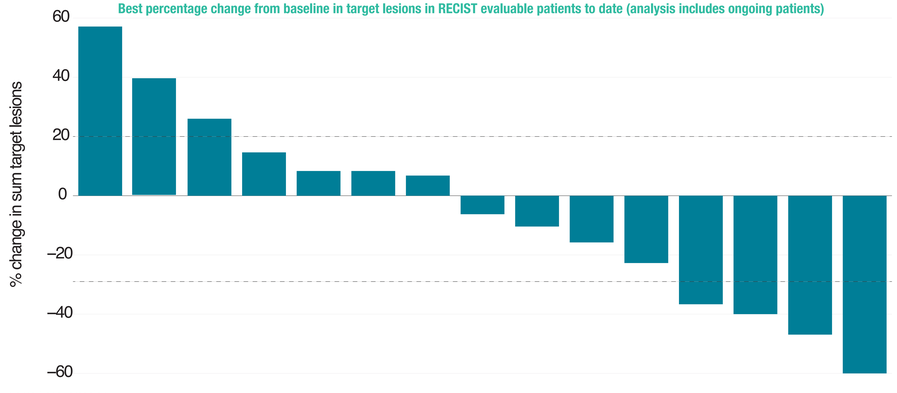
AXL expression by immunohistochemistry



Anti-AXL staining of tumour cells was observed (open arrowheads). Additionally a mainly weak to moderate cytoplasmic staining of stromal cells was seen (arrows).

Efficacy assessment in RECIST evaluable patinets to date - includes patients who are remaining on treatment

Best percentage change from baseline in target lesions in RECIST evaluable patients to date (analysis includes ongoing patients)



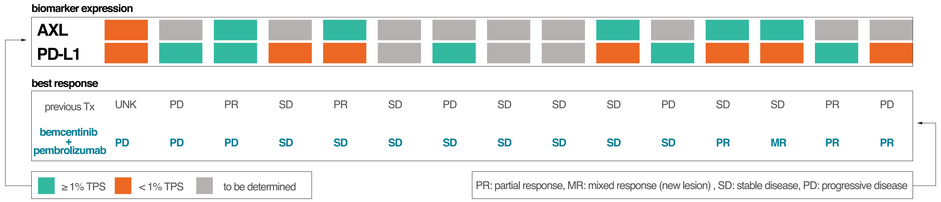


Table 3: Best overall response according to biomarker expression at data cut-off

	PR	SD	PD	N	ORR (%)	DCR (%)
All	3	9	3	15	20	80
PD-L1 ≤ 1%	2	4	1	7	29	86
AXL ≥ 1%	1	3	1	5	20	80

Methods: Plasma protein biomarker levels were measured using the DiscoveryMap v3.3 panel (Myriad RBM) at pre-dose and at C2D1. Bioinformatics analysis was carried out by Fios Genomics. Comparisons were performed on the QC-passed and normalised Myriad datasets.Sum target lesions were assessed as per RECIST v1.1. AXL IHC was performed by Indivumed on pre-treatment FFPE samples using a BerGenBio proprietary immunohistochemistry assay (Davidsen et al). PD-L1 status was determined using a 1% cutoff by IHC using the PD-L1 IHC 22C3 pharmDx assay (Agilent, Carpinteria, CA, USA). Scoring was recorded as percentage of PD-L1-positive tumor cells over total tumor cells in the denominator (TPS).

References

Herbst *et al*: **Lancet** (2015)
Garon *et al*: **NEJM** (2015)
Kang *et al*: **Ann Onc** (2017)
Davidsen *et al*: **AACR** (2018)

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Conclusions

- **The combination of bemcentinib and pembrolizumab exhibits promising activity**
- **Response to treatment was most marked in tumours that were PD-L1 negative and AXL positive**
- **Soluble AXL demonstrates potential as an enrichment strategy**
- **The incidence of Grade ≥3 treatment-related adverse events was low**

This poster was presented at the ASCO Annual Meeting, Chicago, IL (June 1 - 5, 2018)

Analysis of anti-leukaemic activity, predictive biomarker candidates, immune activation and pharmakodynamics in R/R AML and MDS in response to treatment with bemcentinib (BGB324), a first-in-class selective AXL inhibitor, in a phase II open-label, multi-centre study

abstract #: 7020
Poster discussion
11:30 AM - 12:45 PM

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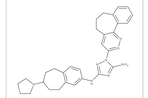
Ph I/II trial in R/R AML and MDS to evaluate safety and efficacy of bemcentinib (BGB324)

Bemcentinib, first-in-class, highly selective orally bioavilable AXL inhibitor in phase II

bemcentinib (BGB324)



Selectivity Profile

	nM	Fold
AXL	0.4	1
Mer	100	250
Tyro	>1000	>1000

Background

Bemcentinib (BGB324) is a first-in-class, oral selective inhibitor of the RTK AXL currently in ph II clinical development across several cancer types. AXL overexpression has been established as an independent negative prognostic factor in AML whereas AXL inhibition via bemcentinib has shown anti- leukaemic activity and immune activation in pre-clinical models of AML and other cancers.

Bemcentinib clinical development

Bemcentinib is being explored as a mono-therapy and in combination with immune-, targeted and chemo-therapy in AML/MDS, NSCLC, TNBC and melanoma across six phase II clinical trials.

AML or high & int-2 risk MDS / pre-viously treated MDS
dose escalation (complete)
- up to 75 patients
- AML unsuitable for int. chemo
- prev. treated MDS, exc del(5q)
- High/Int-2 risk MDS

AML: Single agent; bemcentinib + cytarabine; bemcentinib + decitabine
MDS: Single agent

- Safety
- ORR
- PFS
- OS

BGBC003 (NCT02488408): Phase I/II trial in R/R AML and MDS

AML or MDS (interm-2 and high-risk) patientss received bemcentinib monotherapy in this two part 3+3 dose escalation and cohort expansion study.

BGBC003 demographics

Age (yrs)

Median	74
Range	51 - 85

Type of cancer

R/R AML	32
MDS	5

Gender

Male	22
Female	15

 # Prior therapies

Median	2
Range	0 - 6

Ethnicity

Caucasian	36
African American	1

Safety: TEAEs experienced by > 1 patient

Treatment-related AEs	All grades (n=24)	Grade 3 (n=24)
Total number of treatment-related AEs	**34**	**12**
Total number of subjects with AEs	**13**	**7**
Gastrointestinal disorders	17	6
Investigations	4	2
Blood and lymphatic disorders	3	2
Nervous system disorders	3	1
Fatigue	2	1
Metabolism and nutrition	2	0
Cardiac disorders	1	1
Eye disorders	1	0
Skin disorders	1	0

Dose expansion cohort, all doses. No grade 4 or 5 events.

AXL receptor tyrosine kinase drives tumour survival programme, is negatively regulated by receptor shedding

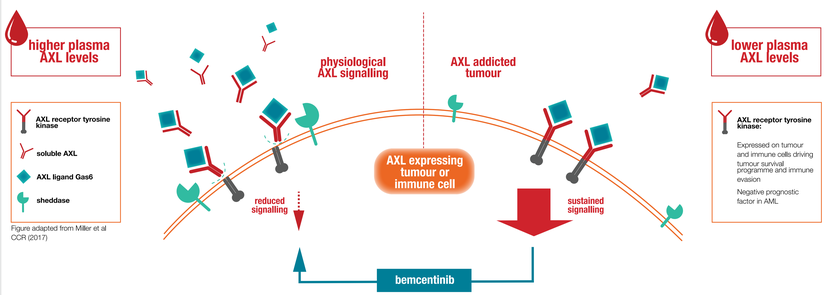
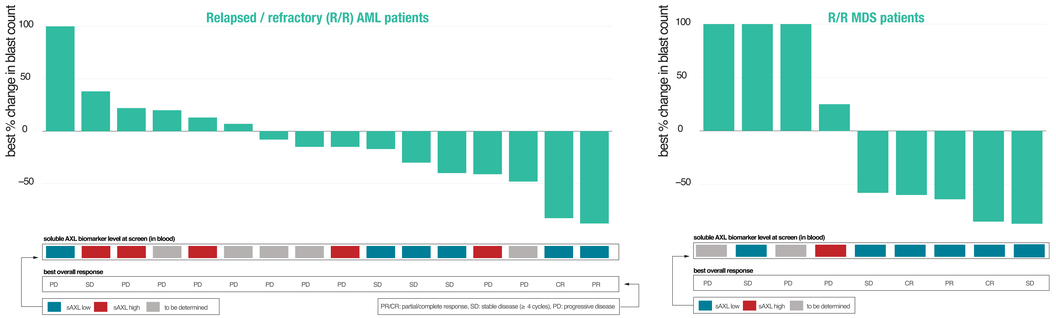


Figure adapted from Miller et al CCR (2017)

Blood and bone marrow plasma levels of AXL correlate with patient benefit

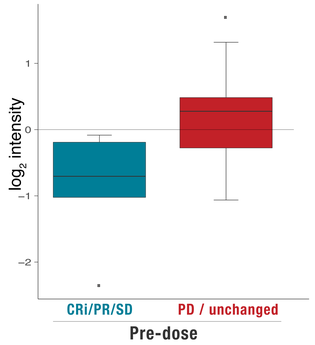
Bemcentinib is active as a monotherapy in relapsed and refractory AML and high risk MDS, particularly in patients with low screen serum AXL levels

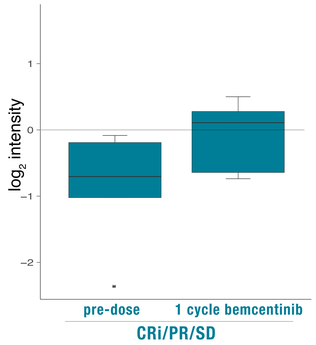


Response assessment per soluble AXL biomarker (measured at screen in blood)

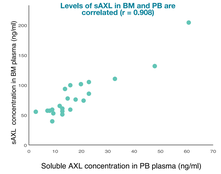
		PD	SD	PR	CR	N	ORR (%)	CBR (%)
AML+ MDS	sAXL high	6	1			7	0	17
	sAXL low	1	6	3	3	13	46	92
AML	sAXL high	5	1			6	0	17
	sAXL low	1	3	2	1	7	43	86
MDS	sAXL high	1				1	0	0
	sAXL low		3	1	2	6	50	100

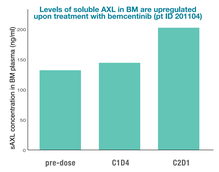
Blood plasma levels of soluble AXL (sAXL) are decreased at screen in patients experiencing benefit, levels increase in response to treatment with bemcentinib





Blood and BM plasma levels of sAXL are correlated & sAXL levels are elevated in BM plasma upon treatment



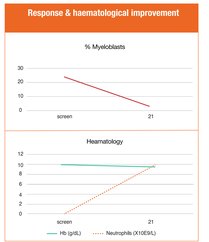


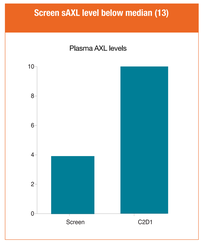
Pharmacodynamic analyses indicate target inhibition & immune activation

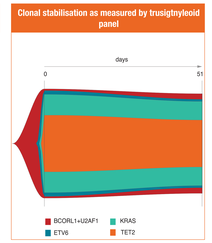
Patient case study

Pt 101-106: relapsed AML, PR on monotherapy bemcentinib

- 68 yo male, white AML patient
- Previously relapsed on azacytidine and melphalan
- PR at C2D1







Conclusions

Serum AXL levels were identified as predictive for patient benefit with an - at time of data cutoff - ORR of 46% and CBR of 92%, respectively, in R/R AML and MDS patients with low serum AXL at screen.

Monotherapy treatment with the selective AXL inhibitor bemcentinib was well tolerated. Treatment emerging adverse events were mainly low grade and reversible.

Primary completion expected for 2018.

Methods

Blood soluble AXL measurements: The DiscoveryMap panel (Myriad RBM) was used to measure blood plasma protein biomarker levels in patients with matched samples available for pre-dose and after one cycle of treatment to identify CDx candidates modulated in response to bemcentinib.

Protein measurements were normalised by calculating the ratio between individual protein levels and the mean of each protein across all samples, before log2-transformation. An assessment of potential confounding factors (gender, age, type of cancer, ethnicity, pre-treatment history, mutation status) was carried out.

Statistical hypothesis testing utilised normalised data as inputs and linear modelling with subsequent Bayesian analysis to identify proteins that are significantly different between sample groups as well as the magnitude of difference (i.e. up- vs. down-regulation). The Bioconductor package limma was used (Ritchie, 2015).

The comparisons tested were: (1) Pts experiencing benefit (CRi, PR, SD) vs. non-responders (PD / unchanged) at pre-dose; (2) paired timepoint comparison, all samples; (3) paired time-point comparison, pts experiencing benefit; (4) paired timepoint comparison, non-responders.

BM soluble AXL measurements: Levels of soluble AXL, a predictive biomarker caididate for treatment with bemcentinib, were measured in patient peripheral blood (PB) plasma as well as bone marrow (BM) plasma using a custom ELISA assay.Tested timepoints inlcuded pre-dose, after four days of treatment and after one cycle of treatment.

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A randomized phase Ib/II study of the selective small molecule AXL inhibitor bemcentinib (BGB324) in combination with either dabrafenib/trametinib or pembrolizumab in patients with metastatic melanoma.

abstract #: 3078

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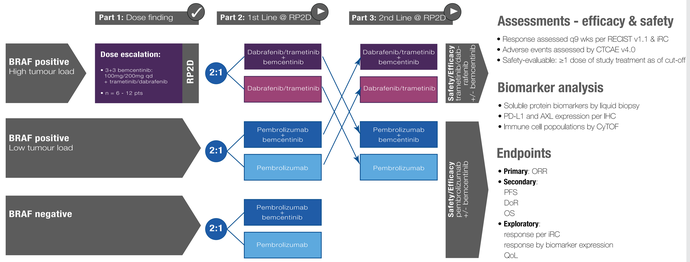
Background & objective

NCT02872259: Ph I/II randomised trial of selective AXL inhibitor bemcentinib in MM patients

Three part randomised design enrolling up to 92 patients



Assessments - efficacy & safety

- Response assessed q9 wks per RECIST v1.1 & iRC
- Adverse events assessed by CTCAE v4.0
- Safety-evaluable: ≥1 dose of study treatment as of cut-off

Biomarker analysis

- Soluble protein biomarkers by liquid biopsy
- PD-L1 and AXL expression per IHC
- Immune cell populations by CyTOF

Endpoints

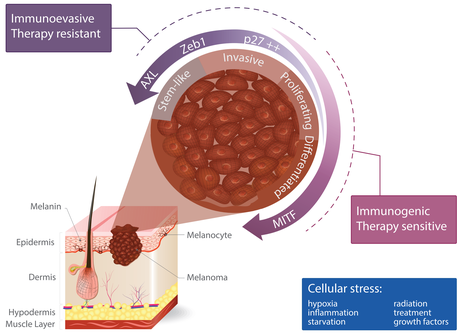
- **Primary**: ORR
- **Secondary**:
  PFS
  DoR
  OS
- **Exploratory**:
  response per iRC
  response by biomarker expression
  QoL

Key inclusion and exclusion criteria

- Histologically confirmed advanced cutaneous non-resectable (Stage IIc) or metastatic (Stage IV) melanoma
- Measurable disease as defined by RECIST 1.1 & documented progression of ≥1 measurable lesion
- Availability of fresh or archival tumour tissue sample suitable for evaluation of predictive biomarkers of response
- ECOG score 0 to 2 at screening
- No prior treatment for Stage IIb or Stage IIc melanoma
- No history of or current active autoimmune diseases
- No symptomatic central nervous system metastatic lesions
- No recent or ongoing systemic treatment with immunosuppressive or immunomodulating agents

Study rationale

The drug resistant low MITF/ high Axl melanoma phenotype is associated with an immune suppressive microenvironment.



Upregulation of the Axl kinase has been associated with reduced response to anti-PD-1 therapy. The drug resistant low MITF/ high Axl melanoma phenotype has been associated with an immune suppressive micro-environment. Axl is a key negative feedback regulator of the innate immune response and attenuates macrophage, dendritic and natural killer (NK) cell activity. Hence, AXL signaling contributes to both tumor intrinsic and microenvironmental immune suppression mechanisms.

Axl dependent cell plasticity signaling pathways confer resistance to inhibitors of BRAF/MEK. Melanomas display either a high E-cadherin/high MITF-M expression on the one hand, or high N-cadherin/high Axl expression on the other. The low MITF/high AXL phenotype is linked to drug-resistance and common among mutant BRAF and NRAS melanoma cell lines. Interestingly, Axl-mediated resistance to BRAF and MEK targeting agents could be predicted by soluble Axl receptor in patient blood samples.

Bemcentinib (BGB324): selective, oral small molecule inhibitor of AXL in phase II clinical testing

Bemcentinib is developed in combination with immune-, targeted and chemotherapy in NSCLC, AML/MDS, melanoma and TNBC.

Selectivity Profile

Kinase	Kinome Scan (Kd)	
	nM	Fold
Axl	0.4	1
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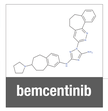
Tyro	>1000	>1000



First part completed, RP2D established: Preliminary interim analysis of RECIST evaluable patients to date, study remains ongoing

Patients

Table 1: Baseline demgraphics

Age, median (range)	65 (34 - 79)
LDH (U/L), median (range)	236 (134 - 3523)
≥ ULN	8 (42%)
< ULN	11 (58%)
Gender, n (%)	
female	9 (47%)
male	10 (53%)
Mutations, n (%)	
BRAF	12 (63%)

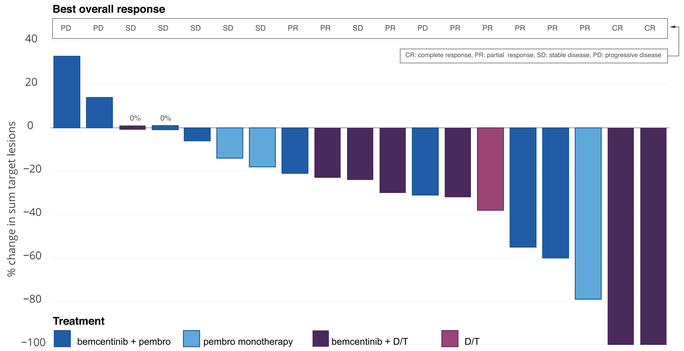
Safety

Table 2: Treatment emerging adverse events - related and non-related to study treatment

System organ class / preferred term	All grades	Grade ≥ 3
Skin & subcutaneous tissue disorders		
Rash	9	2
Gastrointestinal disorders		
Diarrhea	8	0
Constipation	4	0
General & administration site disorders		
Influenza like illness	4	0
Mucositis	8	0
Pyrexia	9	0
Fatigue	11	0
Peripheral oedema	5	0
Nervous sytem disorders		
Headache	2	0
Musculoskeletal & CT disorders		
Arthralgia	2	0
Metabolism & nutrition disorders		
Reduced appetite	3	0
Nausea	7	0
Respiratory disorders		
Dry cough	2	0
Lung embolus	2	2
Investigations		
Weight loss	2	0
Increased QTc	2	0
Increased CPK	2	0
Increased AST/ALT	4	1

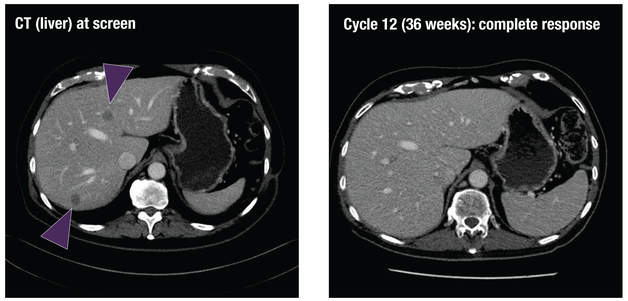
Preliminary efficacy assessment in RECIST evaluable patients to date - includes patients who are remaining on treatment

Best percentage change from baseline in target lesions in RECIST evaluable patients to date



Example CR on bemcentinib + dabrafenib/trametinib

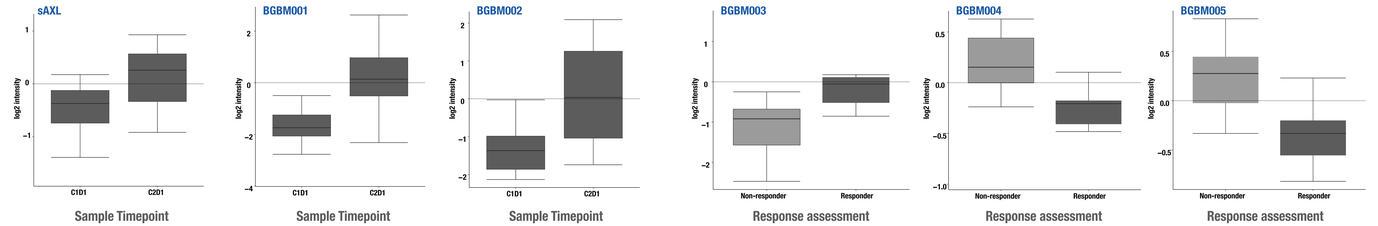
A 68 year old male was randomised to receive 200 mg/daily bemcentinib + standard dabrafenib/trametinib.
At screening the patient had multiple metastases to the liver and the lungs.
At cycle 12, he had a complete response.



Biomarkers

Pharmacodynamics: Serum AXL, serum biomarkers BGBM001 & BGBM002 levels increase upon treatment with bemcentinib

Predictive biomarker candidates: Serum biomarkers BGBM003, BGBM004 & BGBM005 are predictive for patient benefit from combination treatment with bemcentinib



Methods: Plasma protein biomarker levels were measured using the DiscoveryMap v3.3 panel (Myriad RBM) at pre-dose and at C2D1. Bioinformatics analysis was carried out by Fios Genomics. Comparisons were performed on the QC-passed and normalised Myriad datasets.

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Conclusions

- Significant positive response was observed in the majority of patients.
- Blood based biomarkers that predict response have been identified.
- All treatment combinations were well tolerated.
- Safety, efficacy & biomarker performance will continue to be explored.

This poster was presented at the ASCO Annual Meeting, Chicago, IL (June 1 - 5, 2018)

Identification of predictive and pharmacodynamic biomarkers associated with the first-in-class selective AXL inhibitor bemcentinib across multiple phase II clinical trials

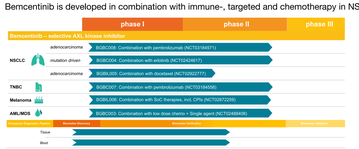
abstract #: 2559

Robert J Holt, David Micklem, Anthony Brown, Murray Yule, Oddbjørn Straume, Sonja Loges, James Lorens; BerGenBio ASA, Bergen, Norway; BerGenBio, Bergen, Norway; Department of Oncology, Hematology, BMT with Section Pneumology and Institute of Tumor Biology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Bemcentinib & AXL biology

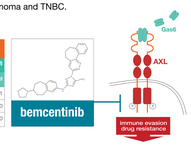
Bemcentinib (BGB324): selective, oral small molecule inhibtor of AXL in phase II clinical testing

Bemcentinib is developed in combination with immune-, targeted and chemotherapy in NSCLC, AML/MDS, melanoma and TNBC.

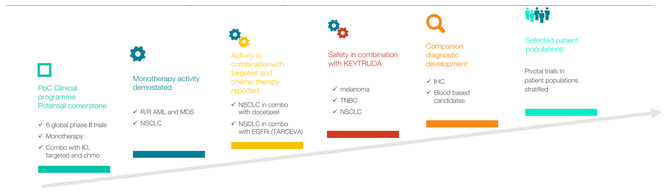


Selectivity Profile

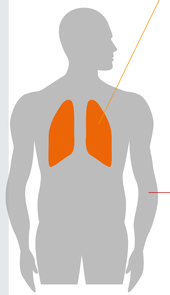
Kinase	Kinome Scan (Kd)	
	nM	Fold
Axl	0.4	1
Mer	100	250
Tyro	>1000	>1000



Bemcentinib clinical development summary



Materials & methods



Tumour tissue biopsy – "the main way cancer is diagnosed"

Methods and materials

- **FFPE tumor samples were analysed from BGBC007 and BGBC008 using a modified NeoGenomics MultiOmyx ™ technology to evaluate the expression of a panel of 13 biomarkers including Axl, CD3, CD4, CD8, CD20, CD56, CD68, CD45RO, FOXP3, CTLA4, PD1, PDL1 and tumor segmentation marker PanCK. The staining was performed using a single 4uM FFPE slide. Within each staining round, two cyanine dye-labeled (Cy3, Cy5) antibodies were paired together and recognized two markers. The staining signal was then imaged and followed by novel dye inactivation, enabling repeated rounds of staining. Proprietary deep learning based workflows were applied to identify individual cells and perform cell classification for all individual markers. Individual cell classification results were combined to generate co-expression summaries and compute spatial distribution statistics for phenotypes of interest.**
- **Axl IHC was performed by Indivumed on pre-treatment FFPE samples from BGBC007 and BGBC008 using the rabbit monoclonal anti-AXL antibody clone C89E7 (Cell Signaling Technology)**
- **The Agilent (Dako) PD-L1 IHC 22C3 pharmDx kit was utilized to evaluate the protein expression of PD-L1 (NeoGenomics). Evaluation was performed using three 4uM FFPE slides, one stained as H&E, one as PD-L1 22C3, and one as a negative control. IHC slides were air-dried and then placed in a 60°C oven for 60 minutes. Epitope retrieval was performed using an Agilent PT Link filled with low pH target retrieval solution set at 97°C for 20 minutes. After conditioning the slides in wash buffer for five minutes, slides were loaded onto an Agilent Autostainer Link 48. Peroxidase blocking for five minutes was followed by incubation with the primary antibody and a secondary linker reagent for 30 minutes each. PD-L1 staining was detected with an anti-mouse and anti-rabbit HRP reagent (30 minutes) and visualized with DAB+ chromogen (10 minutes). DAB staining was enhanced with a copper based enhancer (5 minutes). Slides were then counterstained with FLEX Hematoxylin for 5 minutes and then dehydrated and coverslipped.**

BGBIL006
BGBC007
BGBC008

Liquid biopsy – emerging technology

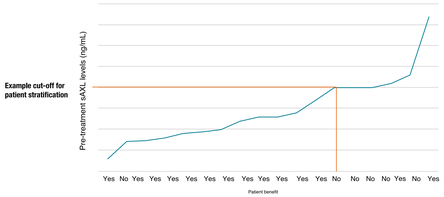
Methods and materials

- **Plasma protein biomarker levels were measured using the DiscoveryMap v3.3 panel (Myriad RBM) in a selection of patients pre-dose and at C2D1 across six clinical trials (bemcentinib monotherapy in AML/MDS (NCT02488460), bemcentinib in combination with pembrolizumab in adenocarcinoma of the lung (NCT03184571), TNBC (NCT03184558) and melanoma (NCT02872259) as well as in NSCLC in combination with erlotinib (NCT02424617) and docetaxel (NCT02922777).**
- **Bioinformatics analysis was carried out by Fios Genomics. Comparisons were performed on the QC-passed and normalised Myriad datasets; 1. Pre-dose (C1D1) Responders vs Non-Responders; 2. Paired Timepoint comparison, C1D1 vs C2D1 for all patients; 3. Paired timepoint comparison, C1D1 vs C2D1 Responders; 4. Paired timepoint comparison, C1D1 vs C2D1 Non-Responders.**

BGBC003
BGBC004
BGBIL005
BGBIL006
BGBC007
BGBC008

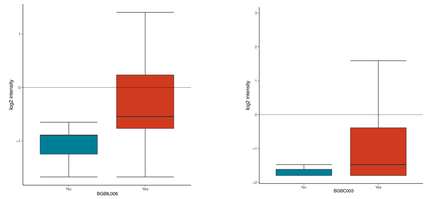
Predictive biomarkers

Identification of soluble AXL biomarkers which are predictive of patient benefit in AML/MDS



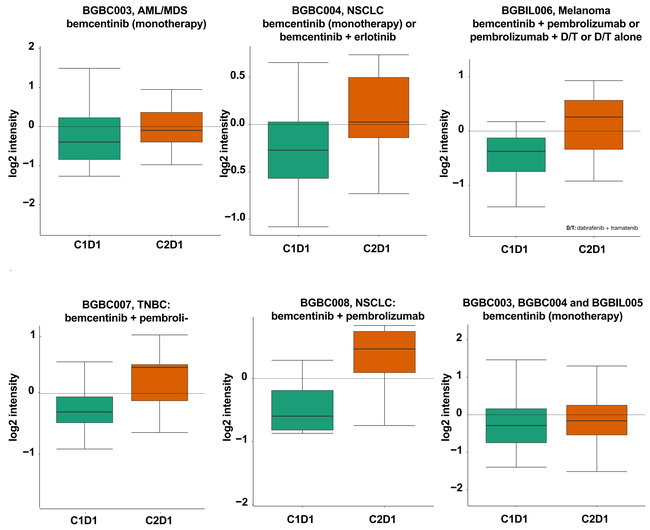
Pre-treatment sAxl levels in plasma samples taken from AML and MDS patients in BGBC003. An example cut-off for patient stratification is presented.

BGBM004: A soluble protein biomarker found to be predictive of patient benefit across several bemcentinib trials

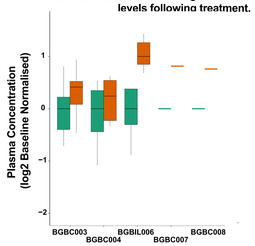


Soluble protein biomarker is predictive of patient benefit in both melanoma and AML/MDS. This marker is expressed on activated T cells and is a member of the TNF superfamily.

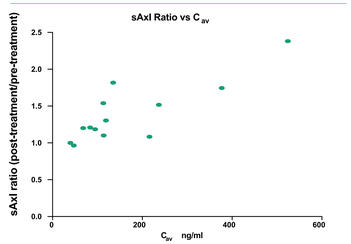
Soluble AXL levels increase following treatment with bemcentinib



sAXL levels C1D1 vs C2D1 in patients showing clinical benefit (log2 baseline normalised). Patients not demonstrating treatment benefit show no significant alteration of sAxl levels followina treatment.



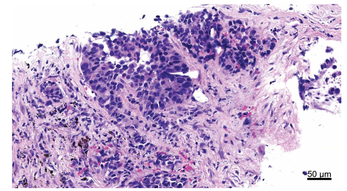
Soluble AXL levels correlate with bemcentinib exposure



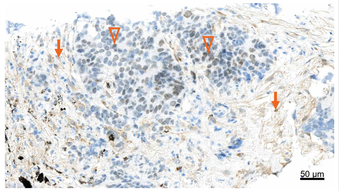
Tissue biomarkers

AXL expression by immunohistochemistry

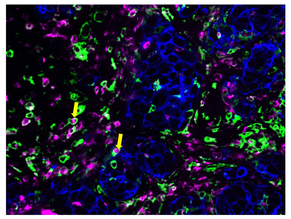
H&E staining



Anti-AXL IHC

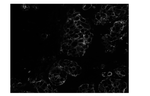


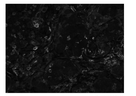
Anti-AXL staining of tumour cells was observed (open arrowheads). Additionally a mainly weak to moderate cytoplasmic staining of stromal cells was seen (arrows).

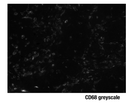


Yellow arrows indicate examples of Axl positive macrophages following treatment.

PanCK+
Axl+
CD68+







- Axl is present in both tumor & tumor infiltrating immune cells
- A significant proportion of Axl expressing cells are macrophages

Conclusions

- sAxl is predictive of patient benefit from bemcentinib monotherapy in AML/MDS
- Other predictive markers have been identified across multiple disease indications
- sAxl increases following bemcentinib treatment in all indications including monotherapy and combinations
- sAxl levels correlate with bemcentinib exposure
- A predictive AXL IHC method is under development
- Axl is expressed in tumor infiltrating macrophages

Acknowledgements

Patients, Investigators, Myriad RBM, Fios Genomics, NeoGenomics and Indivumed

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