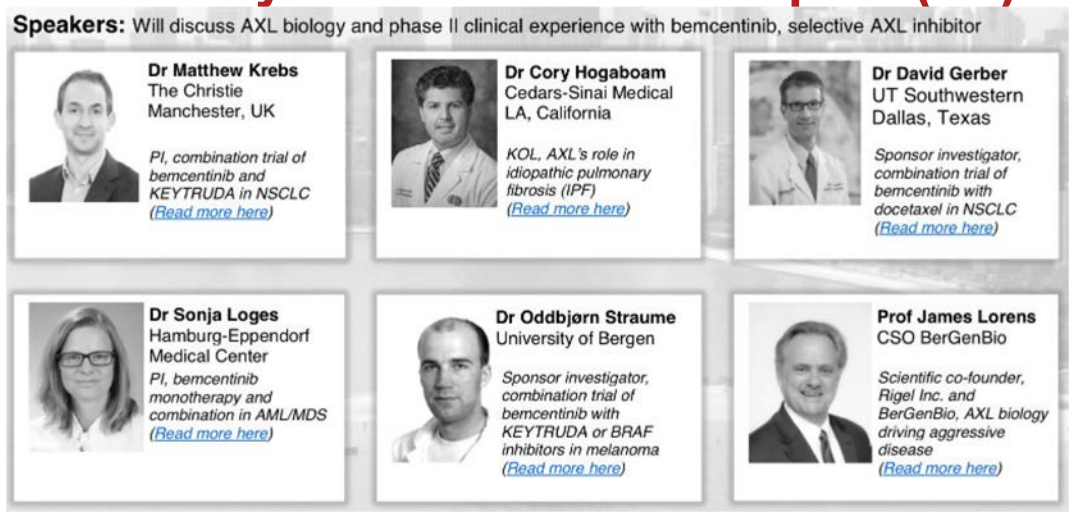
Bemcentinib development program update

ASCO / June 2018

BerGenBio

BerGenBio reception at *ASCO* – 2nd June 2018
Presentation of AXL biology and interim clinical data with bemcentinib

Saturday June 2nd 2018: 6-8 p.m. (CT)



- **BerGenBio KOL reception – 200 attended**

  Short talks by KOLs and PIs

  - AXL biology
  - Bemcentinib interim clinical data

- **BerGenBio ASCO Investor Call: Mon June 4th 8:30am CET**

- **4 poster presentations and discussion at ASCO:**

  Mon June 4th 8am – 11:30am CT

  - Bemcentinib monotherapy in R/R AML, poster 80
  - Bemcentinib KEYTRUDA combo in NSCLC, poster 292
  - Bemcentinib biomarkers, poster 385

  Mon June 4th 11:30am – 12:45pm CT

  - Poster discussion bemcentinib in AML

  Mon June 4th 1:15pm – 4:45pm CT

  - Bemcentinib KEYTRUDA and BRAF combo in melanoma, poster 375

ASCO June 2018 – HIGHLIGHTS

(all Phase II trials are ongoing and results presented are preliminary and subject to change as the trials progress to completion. Updated data will be presented during 2018)

ASCO poster # 385, June 4 8 AM CT

Biomarker programme

- ✓ **AXL IHC:** AXL expression corresponds with patient benefit in KEYTRUDA combo studies
- ✓ **Liquid biopsy:** Soluble AXL is predictive of patient benefit in AML/MDS

ASCO poster # 292, June 4 8 AM CT

Bemcentinib + KEYTRUDA: NSCLC

- ✓ 8 of 15 patients reported tumour shrinkage, including 3PRs at their first scan
- ✓ Assessment by AXL expression:
  - ✓ 5 of 6 evaluable pts were AXL positive,
  - ✓ 4 of those had clinical benefit

ASCO poster # 80, June 4 8 AM CT

Bemcentinib monotherapy: AML/MDS

- ✓ Plasma soluble AXL found predictive of patient benefit
- ✓ 12 of 13 patients reporting sAXL levels below pre-defined threshold at pre-treatment experienced clinical benefit, incl. 3 CR, 3 PR

Bemcentinib + EGFR inhibition: NSCLC

- ✓ 1st Line, 5 of 6 pts report tumour shrinkage incl . 1 PR

Bemcentinib + docetaxel: NSCLC

- ✓ 3 of 7 evaluated patients report PRs

ASCO poster # 375, June 4 1:15 PM CT

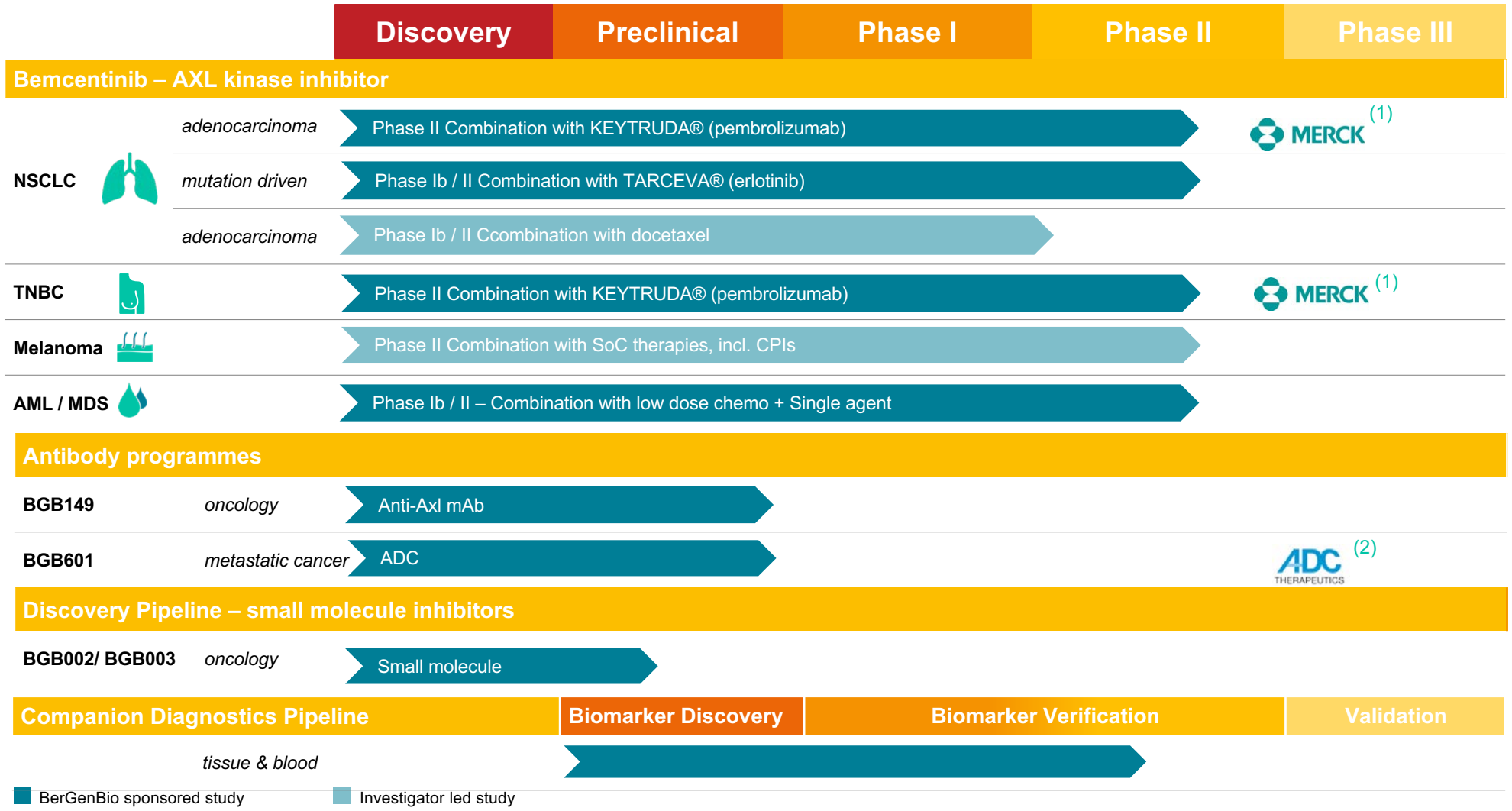
Bemcentinib + KEYTRUDA & TAF/MEK: Melanoma

- ✓ 15 of 19 pts radiographically evaluated to date showed tumour shrinkage incl. CRs, 8 PRs and 6 SDs

Bemcentinib + KEYTRUDA: TNBC

- ✓ 14 of 18 patients were AXL negative and reported no benefit,
- ✓ 12 of 15 patients were PD-L1 negative; 6 were evaluable for efficacy with 1 reporting tumour shrinkage.

Advancing a broad clinical development pipeline



Patients:
>350

Sites in Europe and North America:
50

Key read-outs:
2018

(1): Clinical trial collaboration, no preferential rights (2): outlicensed

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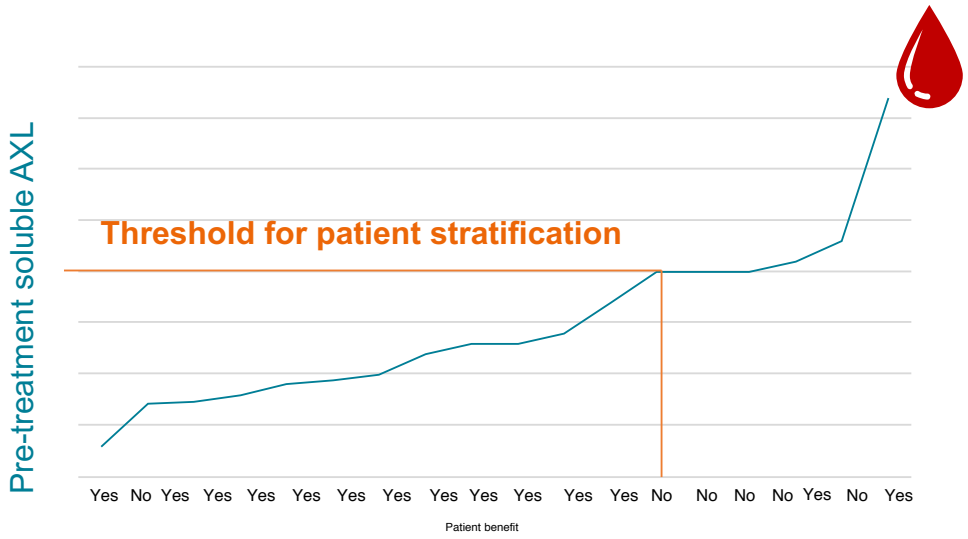
BerGenBio Companion Diagnostics programme

- ✓ Identify biomarkers which predict response to bemcentinib in both tissue and liquid biopsies
- ✓ Biomarkers to be used for patient stratification and companion diagnostic development

Companion diagnostic programme:

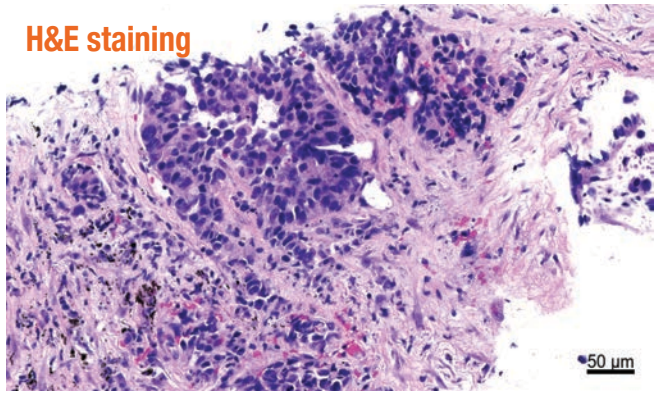
Plasma soluble AXL (sAXL) and other predictive blood based markers
AXL IHC method

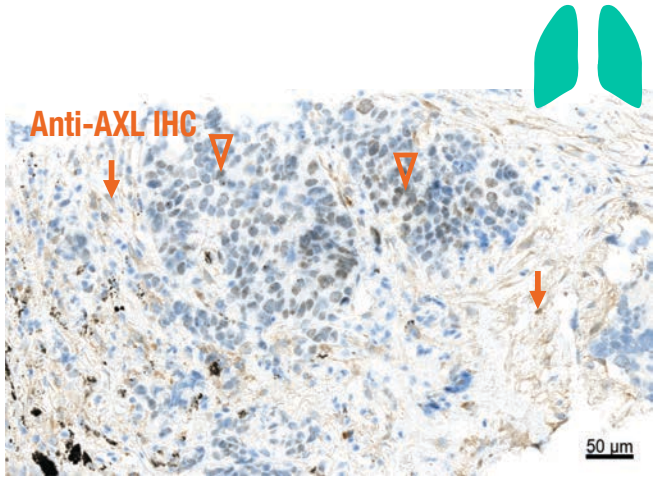
Liquid biopsy: serum AXL levels predict patient benefit to bemcentinib monotherapy in AML



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

IHC assay: Increased benefit in AXL positive patients in KEYTRUDA combo study (BGBC008)





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

Source: ASCO Annual Meeting (June 2018)

BGBC008 trial in NSCLC

KEYTRUDA monotherapy showed 18% response rate in previously treated NSCLC. PD-L1 negative patients remain particularly challenging.

The BGBC008 trials are designed to test the hypothesis whether AXL inhibition can

- **Enhance** responses to immunotherapy when given in combination with KEYTRUDA (pembrolizumab) in previously treated, immunotherapy-naïve NSCLC patients, respectively.

Clinical collaboration with Merck & Co. (MSD)

MERCK

BGBC008: Combination studies with KEYTRUDA

BGBC008 Phase 2 – Adenocarcinoma of the lung

Previously treated, unresectable adenocarcinoma of the lung up to 48 pts any PD-L1 expression any AXL expression no prior IO	**Simon two stage (interim after 22 pts)**	**Single arm** bemcentinib 200mg/d KEYTRUDA 200mg/3w	**ORR**

Status June 2018

- ✓ Tumour shrinkage was reported in 8 of 15 evaluable patients to date, including three PRs and one mixed response,
- ✓ Response assessment according to biomarker expression analysis available thus far:
  - 6 of 7 PD-L1 negative patients reported clinical benefit, including 2 PR and 2 patients with evidence of tumour shrinkage.
  - 5 of 6 patients thus far tested for AXL expression with BerGenBio's proprietary immunohistochemistry assay, were AXL positive.
  - 4 of 5 Axl positive patients reported clinical benefit including 1 PR and 2 patients with evidence of tumour shrinkage.
  - All 4 AXL positive patients reporting clinical benefit were found to be PD-L1 negative.
- ✓ An acceptable safety profile of the combination was reported with only a minority of patients experiencing fully reversible adverse events.

BGBC008: NSCLC Combination study with KEYTRUDA
Preliminary interim analysis: significant benefit observed
correlation with AXL expression, particularly encouraging results in PD-L1 negative patients

	PR	SD	PD	N	ORR (%)	DCR (%)
All	3	9	3	15	20	80
PD-L1 < 1%	2	4	1	7	29	86
PD-L1 ≥ 1%	1	2	2	5	20	60
AXL < 1%			1	1	0	0
AXL ≥ 1%	1	3	1	5	20	80

Methods: 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).

Analysis includes ongoing patients

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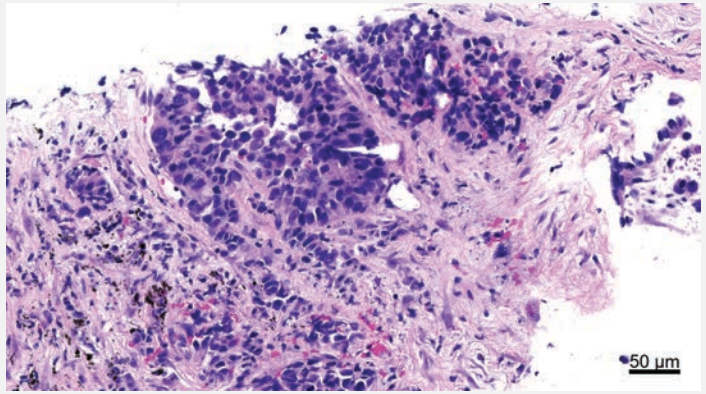
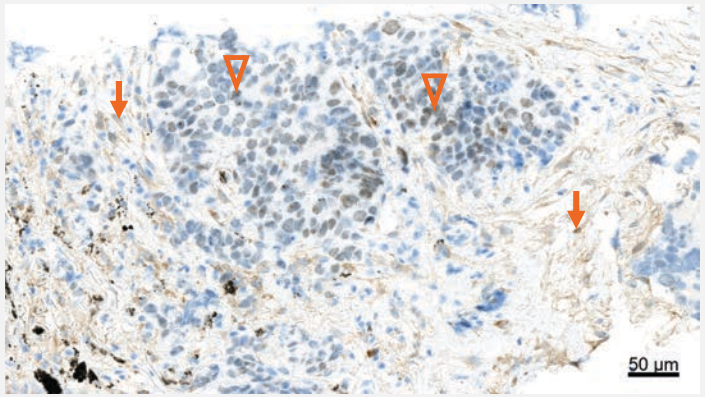
AXL is expressed in a proportion of patients, some of whom have experienced benefit

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).

Axl IHC: first 10 patients	# Pts
Negative (H-score =0)	4
Positive (H-score >25)	6

Patient folio:

AXL positive, PD-L1 negative pt with PR

- 74 year old white male, screen ECOG of 2, liver metastases present
- 1 line of previous therapy with best response of SD
- biomarker expression, TPS (%)
  - AXL: 25%
  - PD-L1: 0%

H&E: haematoxylin and eosin

BGBC007 trial in TNBC

KEYTRUDA monotherapy showed 4% response rate in previously treated TNBC patients.

The BGBC007 trial is designed to test the hypothesis whether AXL inhibition can

- **Enhance** responses to immunotherapy when given in combination with KEYTRUDA (pembrolizumab) in previously treated, immunotherapy-naïve TNBC patients, respectively.

Clinical collaboration with Merck & Co. (MSD) MERCK

BGBC007: TNBC combination studies with KEYTRUDA

BGBC007 Phase 2 – TNBC

Previously treated, unresectable or metastatic TNBC

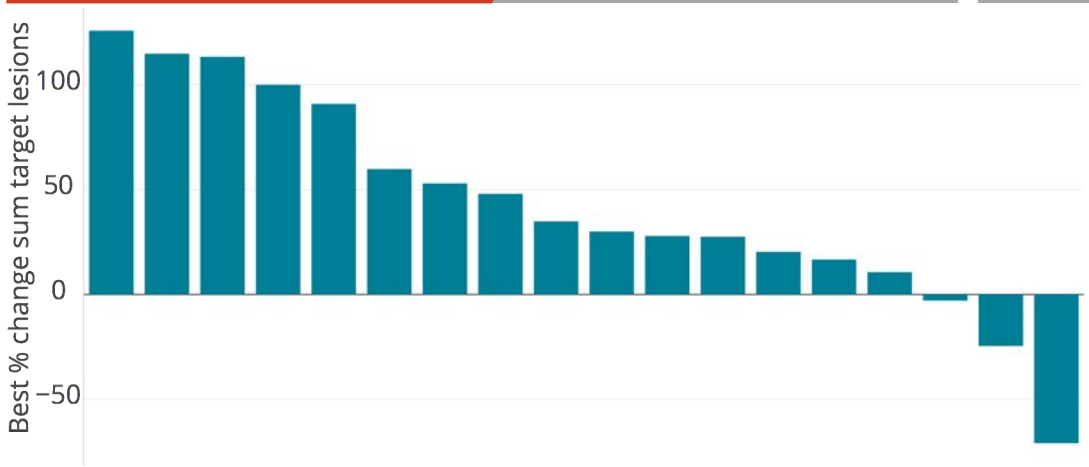
up to 56 pts
any PD-L1 expression
any AXL expression
no prior IO

Simon two stage (interim after 28 pts)

Single arm

bemcentinib 200mg/d
KEYTRUDA 200mg/3w

ORR



June 2018 Status

- 14 out of 18 patients analysed stained negative for AXL
- 12 out of 15 patients analysed stained negative for PD-L1 (<1% TPS)
- Of 18 patients analysed, 1 had a partial response

BGBC003 trial in AML/MDS

AML and high-risk MDS patients unfit for high intensity chemotherapy remain a very challenging patient population with no treatment options when driver mutations are absent

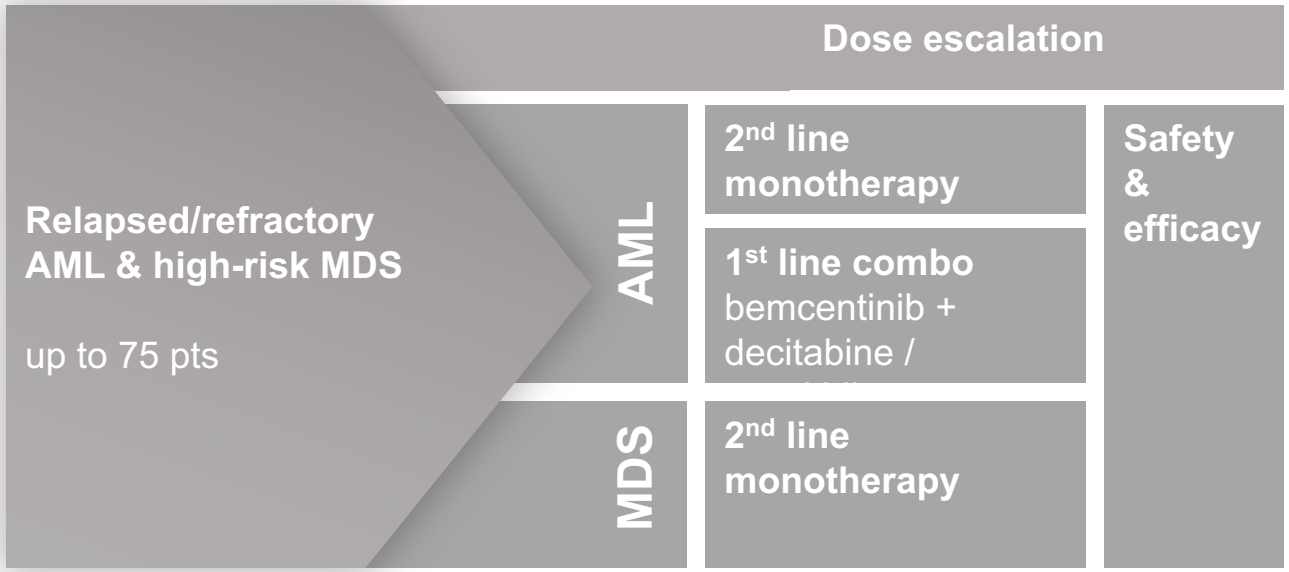
The BGBC003 trial is designed to test the hypothesis whether AXL inhibition with bemcentinib can

- Elicit **single agent** effect and / or
- **Enhance responses** to low dose chemotherapy

when given as a single agent in relapsed / refractory AML and high risk MDS or in combination with azacitidine or decitabine in treatment naïve AML patients

BGBC003: Phase Ib/II trial in AML/high risk MDS

Bemcentinib monotherapy and/or in combination with chemo



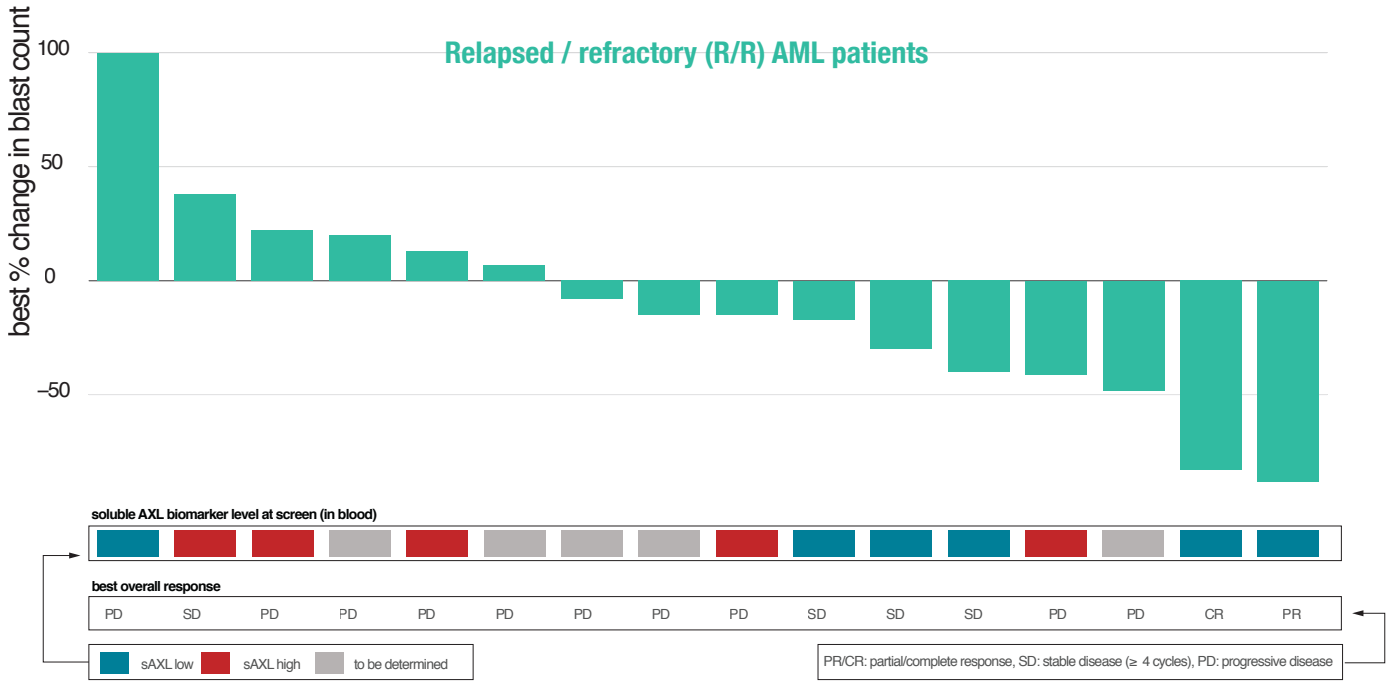
June 2018 Status

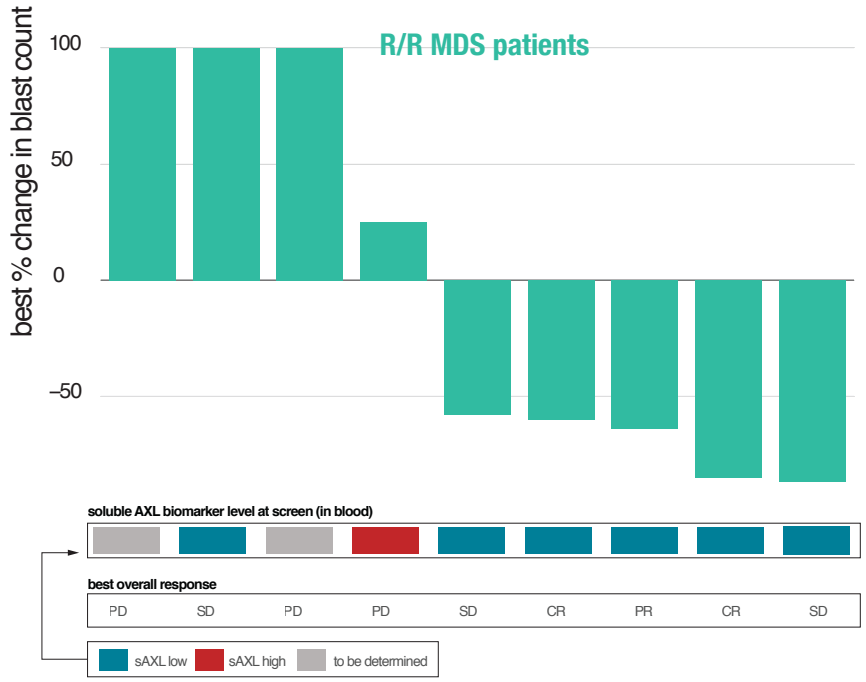
- ✓ Superior response rates to bemcentinib monotherapy in relapsed/refractory (R/R) acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS) could be predicted by soluble AXL (plasma sAXL) levels as determined by liquid biopsy (study BGBC003):
  - 20 R/R AML and MDS patients who were evaluable for response were analysed for pre-treatment plasma sAXL
  - 12 of 13 patients reporting sAXL levels below pre-defined thresholds at pre-treatment experienced clinical benefit, including 3 Complete Remissions, 3 Partial Remissions.
  - 6 of 7 patients with sAXL above the threshold experienced a best response of progressive disease.

Source: NCT02424617

Superior efficacy in low sAXL patients

Bemcentinib is active as a monotherapy in relapsed and refractory AML and high risk MDS, particularly in patients with low pre-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

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BGBC004 trial in NSCLC

NSCLC patients tend to initially respond well to targeted therapies but virtually all acquire resistance over time.

The BGBC004 trial is designed to test the hypothesis whether AXL inhibition can

- **Reverse** and / or
- **Prevent** resistance to EGFRm targeted therapies

when given in combination with erlotinib in EGFRm NSCLC patients who have either progressed on or have just started EGFRm targeted therapy

BGBC004: Phase Ib/II trial in NSCLC of bemcentinib with TARCEVA® (erlotinib)

Stage IIIb or IV disease EGFR mutation positive

Dose escalation & expansion (ongoing)

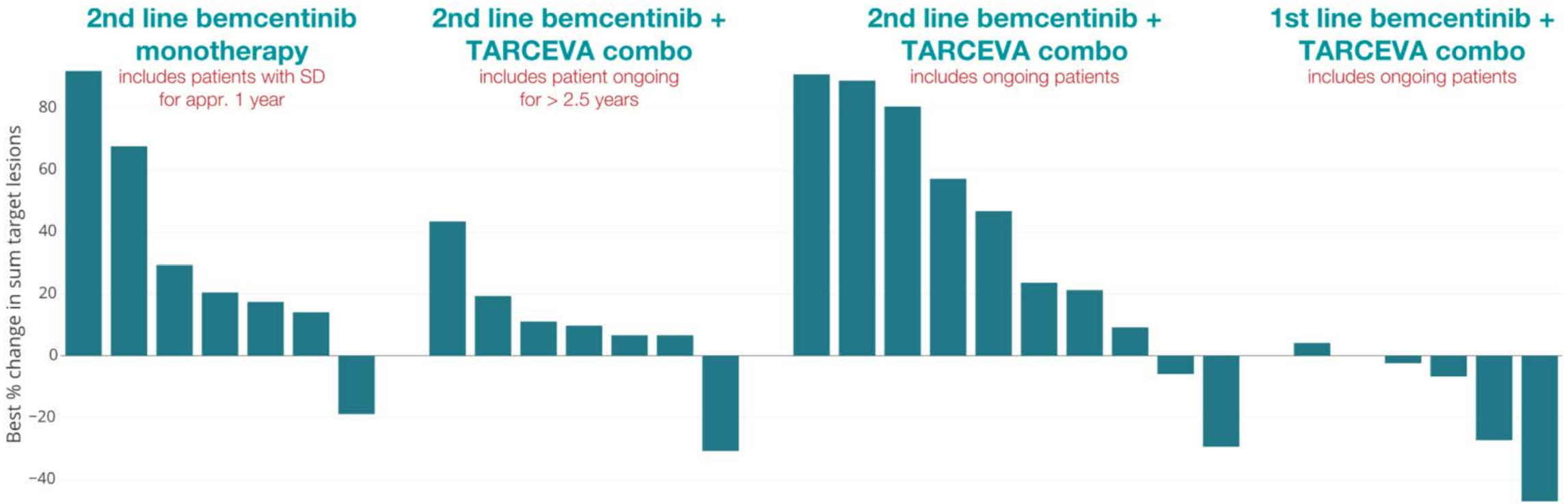
Phase Ib	**Heavily pre-treated** **Arm A1:** bemcentinib monotherapy **Arm A2:** Dose finding in combination	**Safety & efficacy**
Phase II	**Arm B: 2nd line** *Resistance reversal* **bemcentinib 200mg daily + erlotinib daily**	
Phase II	**Arm C: 1st line** *Resistance prevention* **bemcentinib 200mg daily + erlotinib daily**	

June 2018 Status

- ✓ **Arm A1 - monotherapy: 25% CBR**
  2 SD including tumour shrinkage (19%) n=8
- ✓ **Arm A2– combination with erlotinib: 50% CBR**
  1 PR and 3 SD n=8. PR ongoing in excess of 2 years
- ✓ **Arm B – 2L / combo w/ erlotinib: 33% CBR**
  First efficacy endpoint met
  1 PR & 2 SD n=9
- ✓ **Arm C – resistance prevention combo w/ erlotinib:**
  Ongoing and recruiting, 1 PR reported

Source: NCT02424617

PoC for resistance reversal to EGFR inhibitor therapy achieved, prevention of resistance (1st line) ongoing with 1 PR + 4SD (n=6) thus far



Monotherapy effect seen in last line patients:
2 out of 8 patients stable for appr. 1 year

Evidence of reversal of erlotinib resistance seen, combo well tolerated:
- ✓ 2 PRs + 5 SDs (6 wks), includes T790M negative patients, (n=17)
- ✓ Durable responses, including one ongoing patient > 2.5 years

1L combo in pts stable on erlotinib:
- ✓ 1 PR
- ✓ 4SD (n=6)

BGBIL005 trial in NSCLC

Docetaxel is standard second line chemo in NSCLC patients without activating mutations or low PD-L1 expression and common last line treatment option. Response rates are low and PFS short.

The BGBIL005 trial is designed to test the hypothesis whether AXL inhibition can

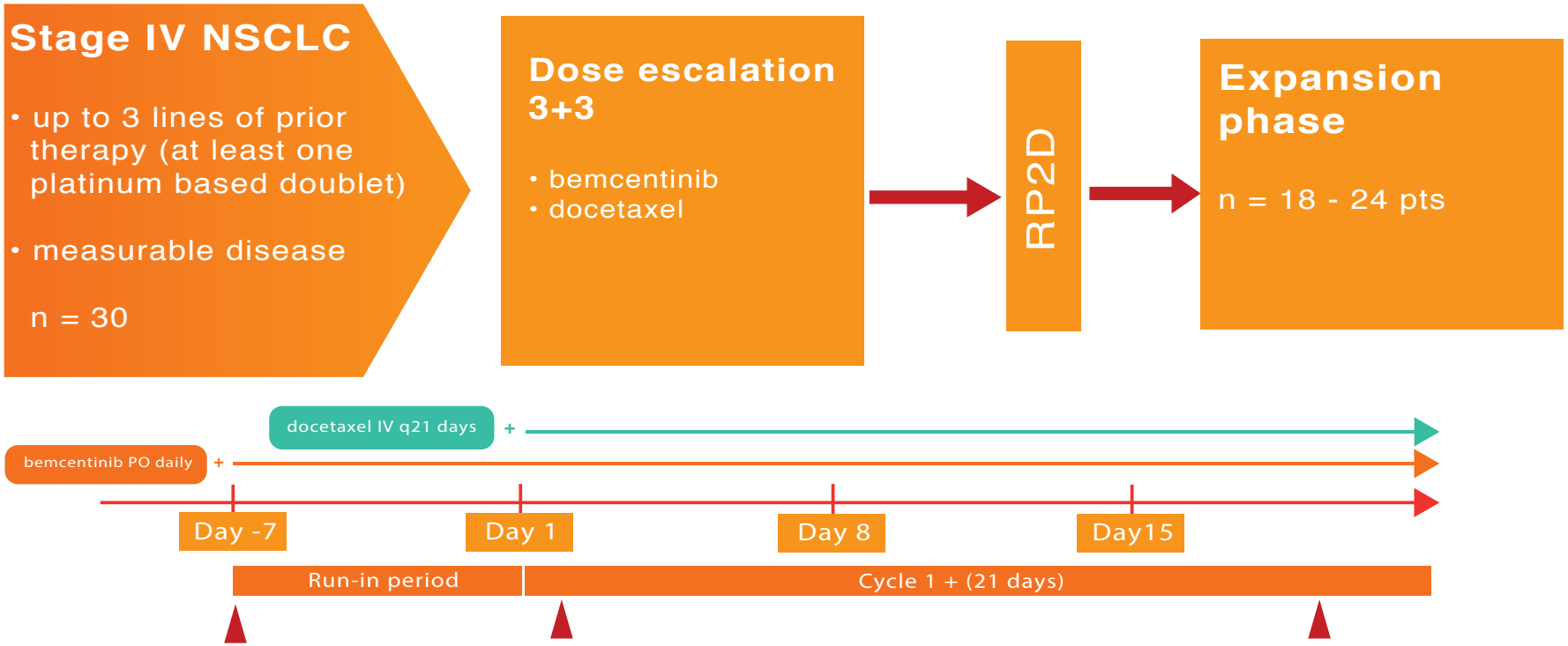
- Enhance responses to chemotherapy

when given in combination with docetaxel in previously treated (last line) NSCLC patients

BGBIL006: Phase Ib/II trial with bemcentinib and docetaxel in NSCLC

Sponsor Investigator: Dr David Gerber, UTSW Dallas

"It is important to remember that most patients with lung cancer will eventually be treated with chemotherapy and for most patients, the benefit from chemotherapy is suboptimal."



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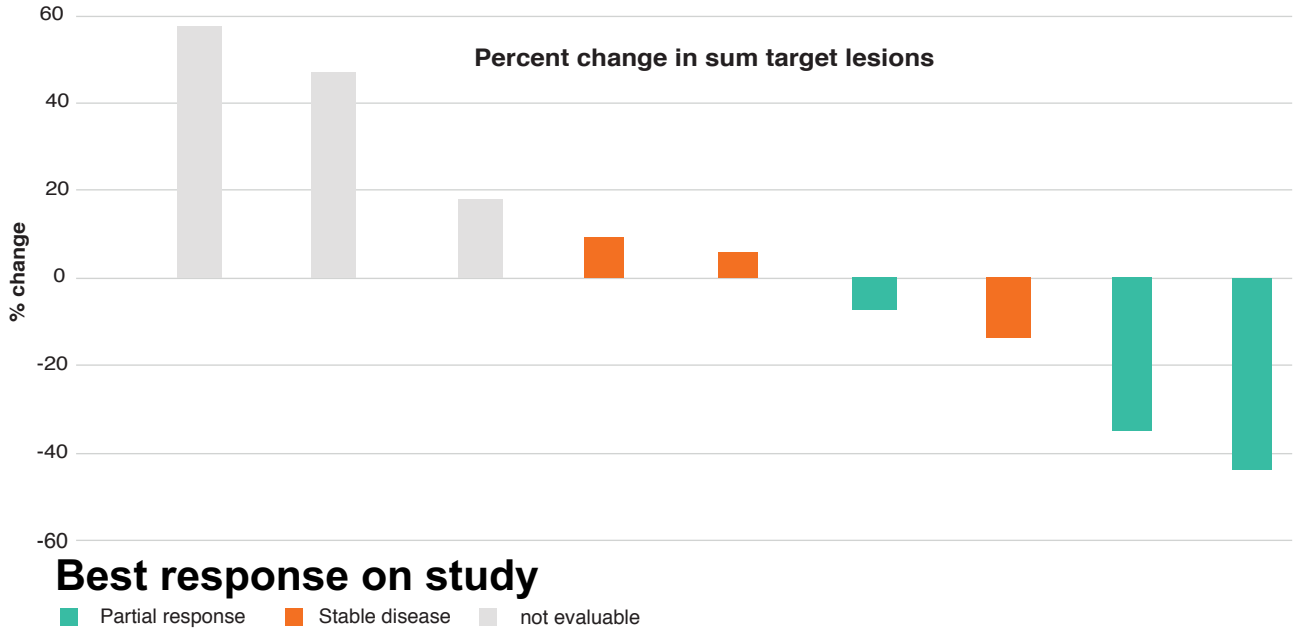
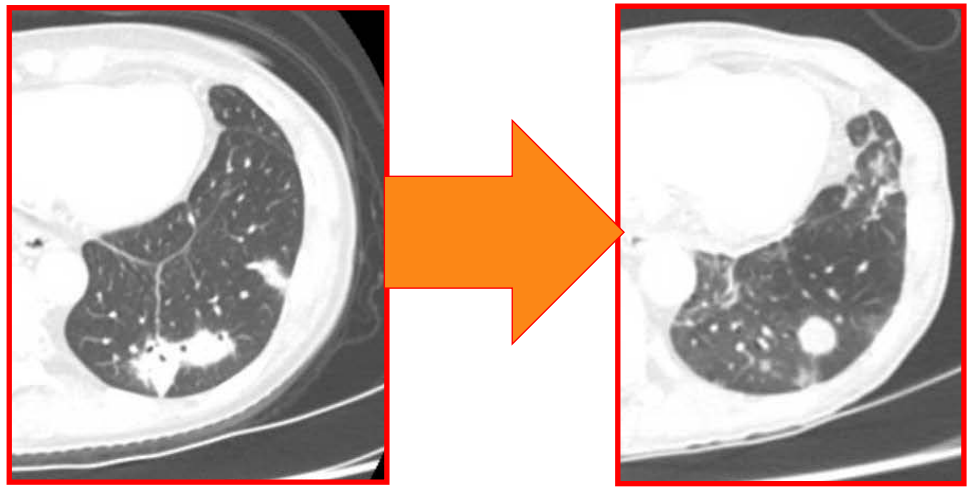
Majority of evaluable patients experience benefit

Includes checkpoint inhibitor failures

Pt	010	008	007	005	009	011	002	006	004
Last treatment	S1 (investigational)	Pembrolizumab	Pembrolizumab	Carboplatin/ pemetrexed	Nivolumab	Gemcitabine	Nivolumab	Nivolumab	Pembrolizumab
Best response to last Tx	SD	PD	PD	PD	PD	PD	SD	SD	PD
Best response on study	NE	NE	NE	SD	SD	PR	SD	PR	PR





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BGBIL006 trial in melanoma

Although responses to TKIs are rapid, resistance ultimately emerges. Monotherapy checkpoint inhibitor responses can be further improved.

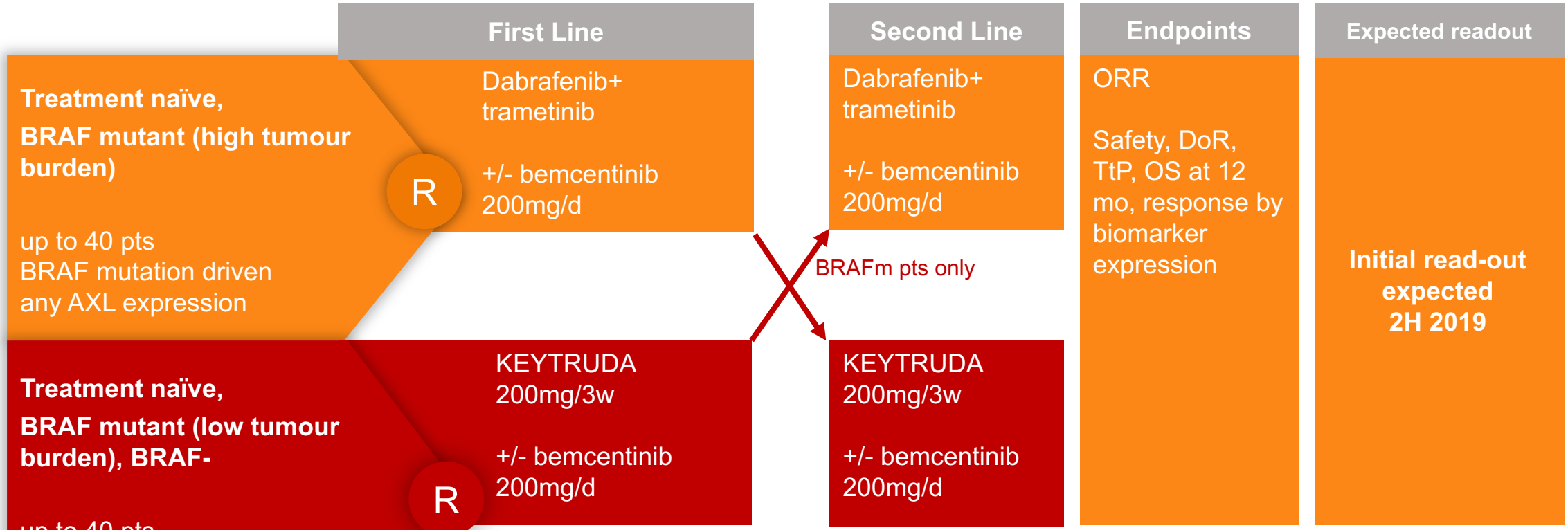
The BGBIL006 trial is designed to test the hypothesis whether AXL inhibition can

- **Enhance** responses to immunotherapy
- **Enhance** responses to targeted therapy

when given in combination with pembrolizumab or dabrafenib/trametinib in treatment naïve melanoma patients

BGBIL006: Randomised Phase II trial of bemcentinib in combination with targeted and I/O therapies in Melanoma

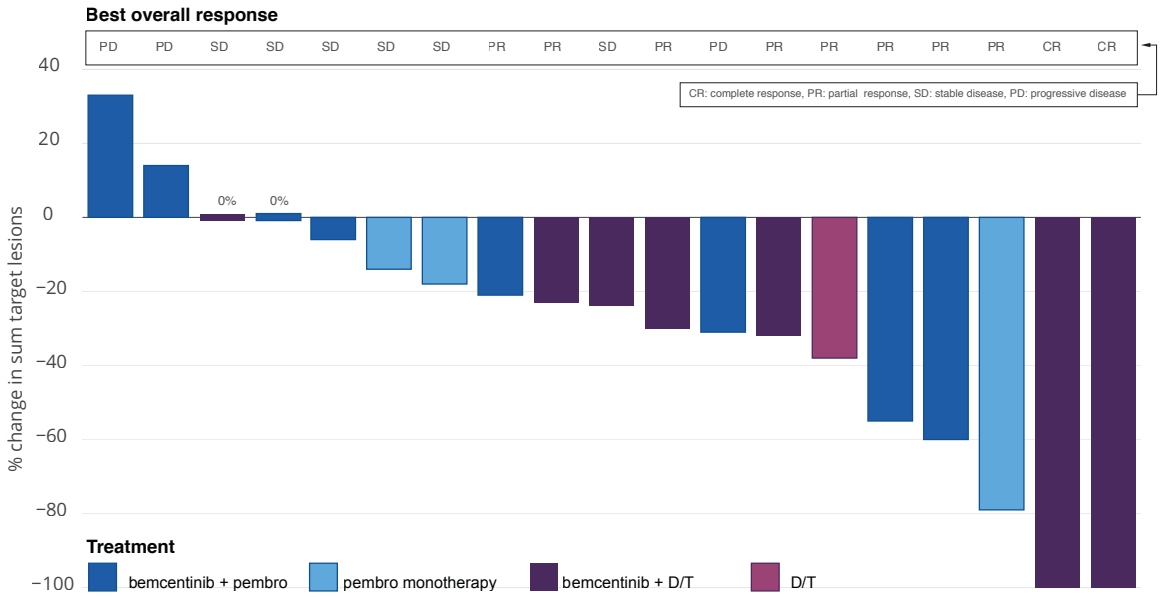
Melanoma, randomised SoC (KEYTRUDA or BRAF/MEKi) +/- bemcentinib



Source: Straume *et al* World Conference on Melanoma (October 2017)

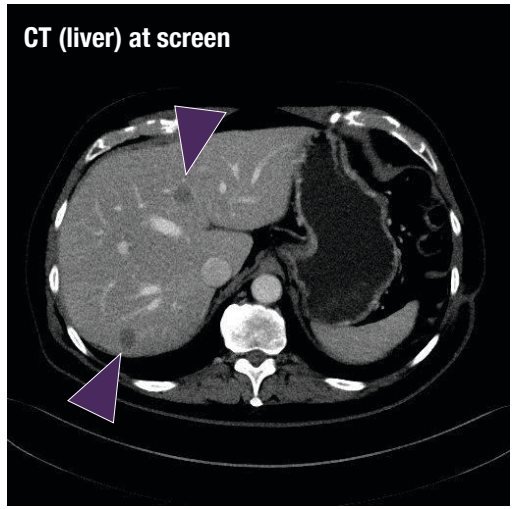
Both combos are well tolerated, and encouraging responses are seen

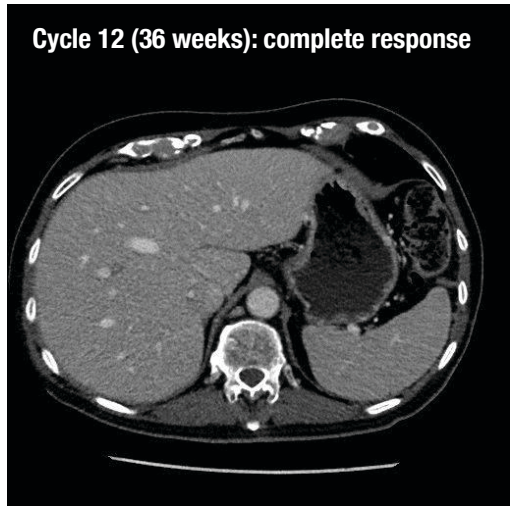
Best percentage change from baseline in target lesions in RECIST evaluable patients to date



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.





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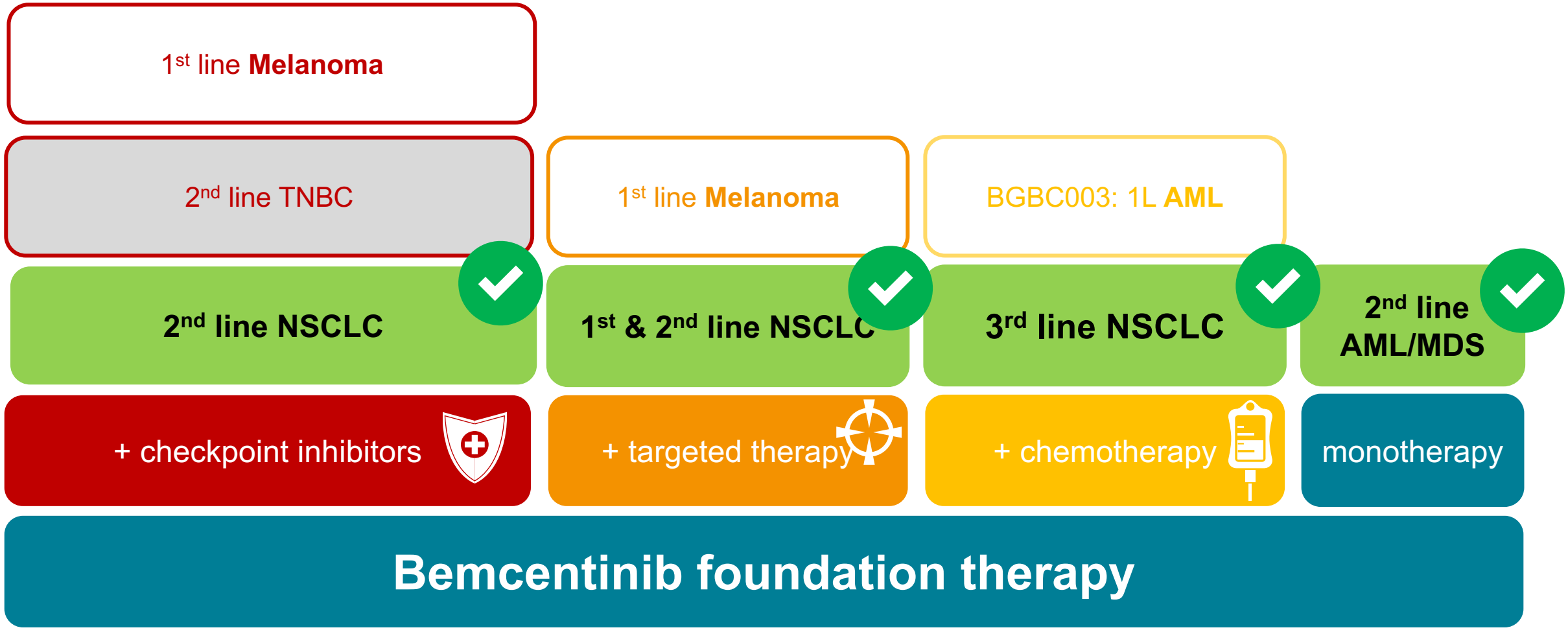
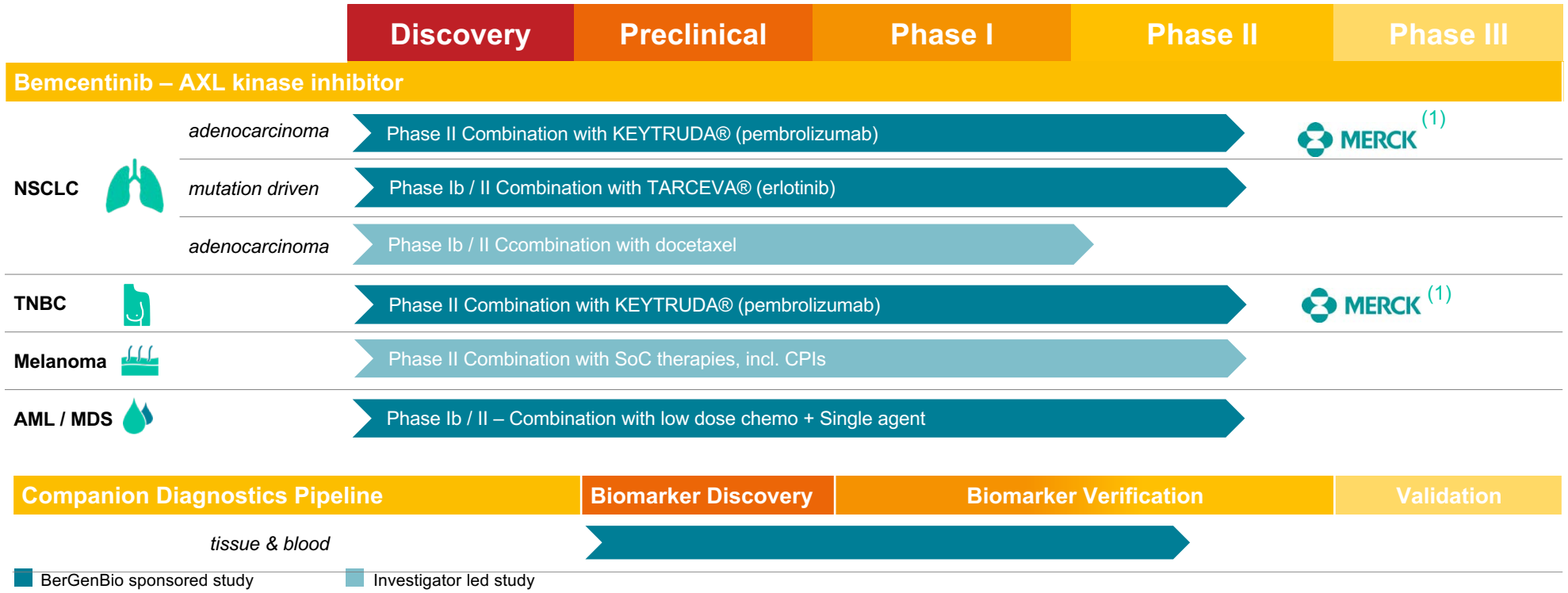
Bemcentinib recently reported Proof of Concept Phase II data



Ongoing phase II clinical development



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